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TWENTIETH CENTURY

PRACTICE

AN INTERNATIONAL ENCYCLOPEDIA

OF

MODERN MEDICAL SCIENCE

BY

LEADING AUTHORITIES OF EUROPE AND AMERICA

EDITED BY

THOMAS L. STEDMAN, M.D.

NEW YORK CITY

IN TWENTY VOLUMES

VOLUME II.

NUTRITIVE DISORDERS.

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ADDISON'S DISEASE

AND OTHER

DISEASES OF THE ADRENAL BODIES.

BY

SIR DYCE DUCKWORTH,

LONDON.

ADDISON'S DISEASE, AND OTHER DISEASES OF THE ADRENAL BODIES.

INTRODUCTORY.

I. Anatomy of the Adrenals.

The Supra-renal Capsules* are classified amongst the ductless glands of the body, in common with the spleen, thyroid and thymus glands. These have no excretory ducts. They lie at the back of the abdomen, surmounting each kidney, attached to it by connective tissue, and are behind the peritoneum. They are somewhat triangular in form, flattened from before backward. The right one is shaped like a cocked hat, but the left is somewhat semilunar, and is larger than the right one.

They measure from an inch and a quarter to nearly two inches in length, are less in width, and are two to three lines in thickness. They weigh from one to two drachms each. During the earlier months of fœtal life, the adrenal bodies preponderate greatly in size as compared with the kidneys. This relative proportion tends gradually to diminish toward the end of intra-uterine life, but even then they appear large in comparison with the kidneys. The late Professor Allen Thomson, of Glasgow, was of the opinion that the preponderance of the adrenals in fœtal life was peculiar to the human subject, and not met with in any other mammalian animals.

These bodies are believed by some writers to be of larger size in swarthy than in fair races. This is an error, and the fact is established that there is no noteworthy difference as to size or structure of the supra-renal capsules in the dark or white races of mankind.

The adrenal bodies, although large in early fœtal life, and smaller by far at the time of birth, yet continue to grow with the growth of the body up to the time of adult age.

Before puberty these bodies are firm and partially translucent at

* The supra-renal capsules, or adrenal bodies, are sometimes described as the atrabiliary capsules from the dark-brown hue occasionally observed in their medullary portion after death.

the edges, and they contain a minimum amount of fat at this period. In the adult they are less firm, and never translucent in health; the amount of fatty matter is greater, and appears to go on increasing in advanced life (see p. 27).

The stroma of the glands is formed by prolongations from the outer investing sheath of connective tissue.

On section of healthy glands, there are at once apparent an outer and an inner portion. The outer is termed the cortical, and the inner the medullary portion. The cortical layer is of a yellowish color, the medullary of a pearly aspect, and after exposure to the air this portion is found to become somewhat pink in hue. In the latter may be seen sections of blood-vessels, arteries, and veins.

Three zones are described in the structure of the cortex. The external one is a layer of closed vesicles, the *zona glomerulosa*. The vesicles contain a few small cells and a finely granular grayish material, but no fat-globules.

The middle layer, the *zona fasciculata*, is composed of cylinders invested with a stroma of connective tissue. These tubules are of three kinds, one set containing an opaque refracting mass, probably fatty, and indistinctly appreciable cells with numerous nuclei. A second variety of tubule is of brownish color, composed of finely granular cells containing fat-globules. The third variety consists of gray tubules, filled with cells whose nuclei contain fat-granules. These cylinders measure about $\frac{1}{700}$th of an inch in diameter.

The third layer of the cortex, the *zona reticularis*, is formed by the breaking up of the tubules and the dispersion of their contained elements. The cells are finely granular, and may have no deposit of fat in their interior; but sometimes fat is present, together with large yellow granules, seemingly pigmentary in nature.

The medullary portion consists of a reticular stroma containing groups of irregularly shaped cells. These closed vesicles are not arranged in tubular fashion, and this portion presents a marked contrast to the structure of the cortex. There are elements of the cortical substance, and abundant nervous structures. The cells are poor in fat, and occasionally branched, resembling multipolar nerve-cells. The nerves pass through the cortex, and ramify in anastomosis through the medullary portion. The cells of the medulla are regarded by some observers as nervous, and there are certainly true multipolar nerve-cells among them.

The *blood-vessels* are numerous and imbedded in the trabeculæ. A rich plexus of capillaries invests the cortical portion. The medulla is furnished with a very rich vascular supply of capillaries. The supra-renal arteries arise on each side of the aorta opposite to the

superior mesenteric artery. They pass to the under surface of the organs, anastomosing with capsular branches from the phrenic and renal arteries. In the fœtus these arteries are as large as the renal arteries. The right supra-renal vein opens into the vena cava inferior, and the left into the left phrenic or left renal vein.

Lymphatics.—Lymph-spaces and sinuses exist throughout the organ, but are best seen between the cells of the zona fasciculata. They occupy the intercellular spaces and lacunæ. The lymphatic vessels lie in the capsule and in the connective tissue around the central veins. They are provided with valves, and pass into the lumbar lymph glands.

The nerves to the supra-renal bodies are derived from the renal and solar plexuses, and thus have sympathetic elements in them coming from distant parts, with necessarily dependent wide radial associations and relations. The splanchnic nerves come into relation with the nerve-supply through the solar or epigastric plexus and its semilunar ganglia. The right pneumogastric nerve also terminates in the solar plexus.

The supra-renal plexus is also joined by the phrenic nerves, a ganglion occurring at their junction. The branches of this plexus are remarkably large in relation to the size of the bodies they supply.[1]

From the position of these bodies, they long remain warm in the *cadaver*, full of blood which gravitates toward them, and so are more than many other parts prone to decompose early, and to lose the aspect which is natural to them during life. In fat subjects they are not always easy to find, and are often torn or cut in hasty manipulation in a necropsy.

Very slight pressure will, under these conditions, cause a rupture to occur between the medullary and cortical portions, the latter being of firmer consistence than the former, and so a cavity is not seldom found in their interior which may wrongly be assumed to have been present during life.

In cases of congenital absence of one kidney, it is usual to find a supra-renal body in its proper situation. This fact plainly indicates that there is no embryological connection between the kidney and the adrenal body, and that they are thus physiologically distinct.

II. Functions of the Adrenals.

Nothing is definitely known as to the functions exercised by these bodies. They are classed with the ductless glands, and commonly believed to form part of the lymph-system of the body. Neither from physiological experimentation nor from pathological investigation has much light been as yet shed upon this subject.

It may be safely affirmed that there was practically no knowledge of any value respecting the diseases of the adrenal bodies till 1855, when Dr. Thomas Addison,[19] of Guy's Hospital, first published his observations on the malady now known by his name.* From that time careful study has been made of the organs, and their grosser diseases are now well recognized. It may further be affirmed that, despite all this knowledge, we still remain in ignorance of the exact functions of these organs in health. We can only surmise that they act most probably as do other ductless glands in the body, and are more particularly a part of the lymphatic system. Without doubt, they bear a remarkable relation to the great abdominal nervous centres, not only lying in close anatomical contiguity to these, but bearing in their intimate textures a larger portion of nervous tissue than is to be found in glands of any kind within the organism.

This latter fact is of prime importance, and can never be lost sight of while considering the morbid anatomy and the symptomatology of all diseases to which these organs are prone.

It is further to be noted that no morbid condition of the adrenals is capable of affording any detectible physical signs during life.† Their size and position almost preclude such a possibility. Their morbid conditions can therefore only be recognized by attention to the clinical symptoms determined by such states, and, as we shall find later on, there may even be no clinical symptoms in some forms of disease of these organs.

Some recent researches by Dr. A. G. Auld, of Glasgow, are of interest in respect of the functions of the adrenal bodies.[2] This observer finds that the blood is almost entirely collected in the inner layer of the cortical zone, and that the cells composing it are more or less pigmented, and highly so in some cases. He finds that many red corpuscles make their way into these cells, and are to be found, by suitable staining, in their interior in all stages of regressive metamorphosis. He believes that certain of these corpuscles are selected and attracted by a chemiotactic action within the phagocyte cells. They then assume a greenish-brown color and begin to break up into larger and smaller particles. The nucleus of the phagocyte is usually much obscured by the pigmenting particles, but it is large and, to-

* In 1837 Rayer wrote that the study of the morbid changes of the supra-renal capsules offered so little that was interesting that it might without detriment be neglected by pathologists, and that it had not thrown any light upon the functions of these organs.

† This is the common experience. In the course of my reading I have met with a record of only one case where a tumor of one adrenal was so large as to be felt during life.

gether with the protoplasm, may show signs of formative activity. Dr. Auld therefore believes that one, at least, of the functions of the adrenals is to destroy a certain class of effete red corpuscles of the blood, and he thinks this is accomplished, possibly, by means of a ferment.

Respecting the medullary portion, he makes out three kinds of cells, namely, (1) glandular columnar or polyhedral cells, faintly eosinophilous, with many large round or oblong nuclei, arranged in the meshes of the reticular stroma; (2) highly branched corpuscles, non-eosinophilous, probably modified nerve-cells; and (3) ganglion cells proper, which cluster round large nerves passing straight through the cortex, and also exist isolated in the reticular meshes. Dr. Auld believes it may be a function of the medullary portion to test the quality of the blood, purified by filtration through the cortex, ere it enters the circulation, and he believes moreover that it may also aid in further reducing effete substances. Examination of the blood after passing through the medulla shows that it has the characters of arterial, oxygenated blood, as it flows through the adrenal veins.

Dr. Auld therefore regards the supra-renal bodies as in part excretory or depuratory glands, and he regards the symptoms of Addison's disease as due to interference with these functions, leading to the circulation of decomposing products of hæmoglobin and a tendency to pigmentary deposition.*

He finds that the cells of the outer cortical zone (zona glomerulosa) are moderately eosinophilous, unlike those in the columns of the middle zone, and that they readily absorb logwood stain. He notes the existence of a central lumen in these columns, filled with secretion, which he thinks is carried away by the lymphatics to minister to certain needs of the organism. The appearance in this outer zone much resembles that found in the anterior lobe of the pituitary body.

Some of his later researches indicate that a substance is to be found, under certain circumstances, which has its origin in the cells of the medulla, and is secreted by them as well as by the lymphatics and blood-vessels. This substance is a colloid of an albuminous character, and Dr. Auld believes that it is essential to the well-being of the blood.

Dr. MacMunn, of Wolverhampton,[3] has made spectroscopic examinations of the cortex and medulla of the adrenals of many animals. In the former he finds the spectrum of histohæmatin, in the latter

* It is to be noted that the results of either partial or total extirpation of the adrenal bodies, even when carefully executed, throw but little light on the cause of Addison's disease. The results are, generally, asthenia, exhaustion, coma, and death. The urine becomes toxic, or its toxicity becomes increased (Kanthack).

that of hæmochromogen. The latter substance he considers to be excretory, and he finds it only in the bile and in the liver. He thus regards the medullary portion of the adrenals as potential for metamorphosis of effete hæmoglobin or hæmatin into hæmochromogen, and suggests that disease of this portion, or removal of it, may entail retention of effete pigment with dispersion or deposit of it in the skin or mucous membranes, or the urine. This is an interesting conception, but it cannot come to our aid with an explanation of the fact that several destructive diseases of the adrenals are quite unaccompanied by the peculiar melasma or pigmentary staining of true Addison's disease.

Dr. MacMunn refers to embryological researches on the adrenals, and quotes Balfour's and Mitsukuri's observations showing that the medullary portion is developed from the sympathetic ganglia, and the cortex from the mesoblast. The former is at first external, but becomes ultimately invested by the latter, although retaining connection with the neighboring ganglia. The bulk of the organ is cortical, and being of mesoblastic origin may be considered as essentially glandular in nature. The extraordinary wealth of blood-vessels is indicative of important functions, and no less is the distribution of the lymphatics, which, according to Klein, is significant of their carrying off some product of the metabolic activity of the glands, for it has been shown that the pigment formed in them is conveyed to the lymph glands which lie in their path. These researches all point to the fact that the adrenals are blood-metabolizing glands. They appear to remove from the circulation useless and worn-out pigments and their accompanying proteids.

ADDISON'S DISEASE.

Without doubt, the most important disease of the adrenal bodies is that now so well known, and generally recognized as "Addison's disease," a disorder which has received the other names, arising from the very noteworthy, and most usually associated symptom of skin-pigmentation, of melasma supra-renale and bronzed-skin disease. This disease was discovered by Addison some years before he published his account of his cases, and was stumbled upon,* as it were, while he was endeavoring to detect the cause of certain fatal cases of anæmia which he encountered from time to time. These cases he tered "idiopathic" to distinguish them from ordinary ones which could be traced to more definite causes such as simple anæmia and

* I find that Addison himself uses this very expression in his original memoir, p. 4.

chlorosis. These idiopathic cases we now recognize as examples of pernicious or grave anæmia, a form of anæmia which is now treated with better success than formerly, although it constitutes always a very grave and often fatal disorder, a hæmopoietic failure. Such cases were indeed taken note of and recorded previously to Addison's researches, in particular by Channing, in New England, in 1842.

To use Addison's own words, "the leading and characteristic features of the morbid state to which I would direct attention are, anæmia, general languor and debility, remarkable feebleness of the heart's action, irritability of the stomach, and a peculiar change in color in the skin, occurring in connection with a diseased condition of the supra-renal capsules." This very concise definition is a masterly one, and no better one can be given now, though forty years have elapsed since it was written.*

Since Addison's time, the disorders associated with his name have received full recognition in all parts of the world. It is happily not a common disease, and there is apparently reason to believe that it is more frequently encountered in hospital than in private practice, and is therefore less common among the upper and well-to-do classes of society.

In respect of its etiology, it is found to occur with far greater frequency in males than in females; according to Dr. Greenhow's inquiries, the relative proportion is as 119 to 64.

It has been met with at all ages from five to fifty years, but the majority of instances occur in men between thirty and fifty years of age.

It is not possible to discover that this malady was known to the older physicians. No descriptions sufficiently attest its definite recognition, and no early museum specimens illustrating disease of the adrenals are known. Possibly the specimens in the Museum of Guy's Hospital from a case of Dr. Bright, placed there before 1846, are the earliest that have been preserved, though their real nature was unknown at the time. The discovery of these is due to Dr. Wilks. The adrenals were overlooked in early autopsies, and were not regarded with any special interest till Addison's researches led to more careful scrutiny of these organs.

Morbid Anatomy.—A knowledge of this is, of course, only derived from specimens of adrenal bodies that have undergone such gross and fully developed changes in the disease as to have led to a fatal issue. Of the earlier changes in the organs in Addison's disease we are quite

* It appears to be an essential factor in true Addison's disease that the adrenals should be more or less destroyed or incapacitated for the discharge of their proper functions.

ignorant, and must be content to remain so. We can only argue from the appearance presented in such cases as come to the post-mortem room. We thus find indications of a progressive morbid process, the earliest stage of which apparently is the formation of new material, firm, whitish, or gray, nodular at the margin, and situated in the medullary portion of the organ. Outlying groups of deposit, much resembling miliary tubercles, are found in close contiguity to the nodules just mentioned.

The latter appear to extend gradually and to encroach upon the cortical portion, causing enlargement and a nodular quality of the entire organ. This may involve more or less of the capsule, and both are commonly invaded, or the entire organ, or both, may be uniformly enlarged as described, and thus be grossly altered in size and texture, although still retaining much of the original anatomical form. Such organs are readily detected. On section, there is no longer any of the normal aspect visible, the medulla and cortex are fused and uniformly involved. The surface is grayish or yellowish, and in parts quite resembles caseous degeneration of tubercular masses. The gray portions are apt to assume a pink tinge on exposure to the air, and this same occurrence is noted, curiously enough, on section of the medullary portion of healthy adrenal bodies, as I have often remarked. The new growths are found to consist of lymphoid cells lying in delicate wavy, fibrillary stroma. These cells are apt to develop into fibroid tissue. The masses thus formed may long remain in this condition before caseation and other changes set in. The caseous degeneration may become so far complete as to soften and liquefy into creamy, puriform matter. A still later stage shows that, as in the case of softening yellow tubercular masses elsewhere, a process of absorption is in progress, and shrinking with obsolescence sets in, leading to small puckered masses, in which calcareous matter is deposited, —so-called cretiform obsolescence.

A chronic inflammatory process simultaneously involves the investing fibrous tissue of each organ, leading to thickening and adhesions to adjacent organs and textures such as the liver, diaphragm, kidneys, pancreas, and, in particular, to the abundant meshes of the solar plexus and semilunar sympathetic ganglia.

Occasionally, marked atrophy, leaving little but firm fibroid tissue, occurs, or nodules of caseous and calcareous matter are noted in the room of natural adrenals.

The disease would appear to begin sometimes in one organ and to advance considerably before it arises in the other, the disease being almost obsolete in one, and in active progress in the other.

The histology of the new growth has been carefully worked out in

all its stages. The grayish translucent substance consists of a fibrillated stroma, containing numerous lymphoid corpuscles. The caseous material consists of amorphous granular matter mixed with shrunken cells, nuclei, and oil. The most recent examinations reveal almost constantly the existence of tubercle bacilli. Gray miliary tubercles have been found, not always containing bacilli, but the latter are more commonly found in the caseous degenerating portions. Tuberculosis may be either primary or secondary to deposits elsewhere in the body and is perhaps more commonly of the latter variety. This is a matter of supreme importance in relation to the whole disease.

Several preparations in the Museum of St. Bartholomew's Hospital plainly give evidence of the tubercular nature of the deposit in the adrenals, both as to intimate structure and the presence of specific bacilli. We have therefore to consider these deposits as essentially of tubercular nature, and we find that they behave in all respects as such deposits do elsewhere, namely, by gradually extending and encroaching, destroying natural tissue, undergoing caseous changes, and setting up proliferation of connective tissue around them with consequent adhesions and matting of adjacent structures.

It appears probable that continued researches into the intimate nature of the specific deposit and changes met with in Addison's disease of the adrenals will render it certain that these are always of tubercular nature, and at the present time it is well-established that tubercular disease is the most commonly associated disorder, being met with in the lungs and in the bones, especially in the spinal column. We may therefore regard this malady as a form of adrenal phthisis. While adopting this view it is necessary to remark that tubercular deposits are, as a rule, not found in these glands in the great majority of cases of pulmonary phthisis due to tuberculosis, even when tubercles due to bacilli are widely spread throughout the organs of the body. These glands therefore resist, somewhat notably, a general tubercular infection. This is certainly remarkable and noteworthy.

Course of the Disease.—The onset is gradual. An impairment of general health is to be noted, and the patient complains of languor and debility. The order of symptomatic development is not uniform. Melasma may, or may not, be an early indication. In dark people this hardly attracts attention. In fair persons the pigmentary alteration is readily appreciable. Melasma may precede any marked change in general health for as long a period as from eight to sixteen months, and it is important to take note of this and seek for other indications of the disease without delay. On the other hand, progressive asthenia, together with indications of cardiac failure and gastric

irritability, may long be the chief symptom noticeable, pigmentation setting in late. A fatal issue has been noted in cases where melasma was entirely absent, the disorder having run its course too rapidly, as it were, for this characteristic symptom to occur. The disease may prove fatal within six or twelve months of the earliest symptoms of failing health. It is rare for the leading symptoms of Addison's disease to continue beyond one year without the onset of more or less melasma.

It is important to know that in the course of the malady there may be remissions and exacerbations in respect of the chief symptoms. In following up cases, this fact has been strongly impressed on my observation, and it affords at least some encouragement in respect of treatment. The end may, however, come very suddenly.

Asthenia is the key-note of the malady. The patient finds it easier to walk about than to stand for any length of time. This is not uncommon in many cases of cardiac debility from any cause. Rest in bed is sometimes imperative, since sitting up may induce syncopal attacks. But even this serious condition may pass off, and the powers revive for weeks or months till a fresh exacerbation occurs.

The cardiac action is singularly feeble, the pulse small in volume and of low tension. Dilatation of the ventricular walls is, however, little, if at all, marked.

Anæmia is present, but not to an extreme degree. There is a general impoverishment of the blood, but no leukæmia.

Dyspnœa is, however, met with, as in anæmia and cardiac debility, also palpitation on exertion, sighing, and yawning.

Gastric irritability is commonly marked, indicated by nausea, hiccough, and vomiting. These symptoms may for a time be the most pronounced of all. The breath is sometimes very fetid.

Wasting is singularly absent in respect of both muscle and fat. The temperature of the body is subnormal throughout the progress of the disease unless active tuberculosis sets in in the lungs, or other intercurrent troubles arise. Addison's disease is apyretic.

Clinical observation fully confirms this fact. But some cases have been noted in which febrile paroxysms occurred. These were generally associated with marked nervous symptoms such as excitement, delirium, drowsiness, loss of consciousness, and convulsions before death.

Dr. MacMunn questions the constant apyrexia of Addison's disease, but the great body of observed facts is against him. In the cases alluded to above, it is sought to explain the fact by supposing that some special toxine was present in the blood. MacMunn quotes the experiments of Foa and Pellacani, who injected aqueous and al-

coholic extracts of the adrenals into rabbits and found most toxic effects, due apparently to the action of some ptomaïne, leading to spinal, bulbar, and respiratory central paralysis and pyrexia. He believes it may be the function of the adrenals to remove from the circulation, and metabolize into a harmless product, this material arising from proteid disintegration, which, when the adrenals are diseased, accumulates in the blood and produces nervous symptoms and pyrexia. Adrenal toxine is believed by MacMunn to be a nitrogenous, non-crystallizable substance. We can only remark with respect to the cases just alluded to that they are exceptional and atypical. They must, however, be remembered by future observers.

It is right to note here that Dr. Duclos, of Tours, expressed the opinion that Addison's disease was due to a general poisoning of the body by pigmentary matter which had not been destroyed by the adrenals.[4] But in opposition to this view we must take note of the fact that cases of acute Addison's disease, ending fatally within a few months, are, as a rule, unaccompanied by characteristic melasma. This point will be referred to later.

The occurrence of rheumatoid pains in the loins and abdomen has been noted with some frequency.

The appetite is capricious, and there may be loathing for animal food. Profuse diarrhœa may supervene toward the end of the malady. There may sometimes be complaint of lumbar pain and of epigastric distress.

With this series of symptoms, every intelligent physician would suspect the onset of adrenal disease, and his opinion should hardly be shaken by the absence of one or more of them.

With the progress of melasma, the patient becomes greatly changed in appearance, assuming the color of a mulatto or of one of the dark races. It varies in degree and in depth of hue on various parts of the body, being usually more pronounced on the exposed parts such as the face, neck, and back of the hands. But it is also found well-marked on the genitals, a sooty hue of the penis and scrotum being very common and characteristic. The groins and axillæ, the nipples and areolæ are apt to become very dark. The tint is never quite uniform all over the body even in an extreme case of "bronzing." As in cases where pigment is apt to be deposited from any cause, points of pressure and those exposed to friction become the seats of greatest attraction in this respect. Thus, the friction of a collar or of braces, constriction by garters, irritation of blisters or sinapisms, or of skin-eruptions, all lead to greater intensity of pigmentation in the sites affected. The patches of varying depth shade off gradually, and have no abrupt margins.

It is well to take note of this fact, because it helps to distinguish *melasma supra-renale* from another morbid condition known as melanoderma, where the pigmentary outlines are sharply defined, and contrast markedly with pale patches void of natural pigment. It is very common to find small spots of dark pigment scattered over the trunk and limbs and on the face, like flat pigmented moles. The contrast of the pearly conjunctivæ with the melasma as seen on the face is very remarkable in a well-developed case of Addison's disease.

This peculiar pigmentation is not, however, confined to the integuments of the body. It occurs on mucous membranes, and is especially to be looked for on the buccal surfaces. Along the inner surfaces of the prolabia and opposite the lower incisor teeth may be noted dark pigmentary patches, and the same are seen on the inner surfaces of the cheeks along the teeth, and on the margins of the tongue.

These much resemble the deposits of pigment met with in the same situations, but more extensively and especially on the palate, in many dogs, when they are reckoned marks of good breeding; they occur in some dark races of men. It is doubtful whether pigment is ever deposited in any internal organs in Addison's disease. The pia mater was once noted to be darker than usual over the medulla oblongata by the late Dr. Carrington of Guy's Hospital.

There is nothing specially noteworthy about the anatomical position of the pigment in these cases. It occurs just where it is usually found in dark races, that is, in the deep layers of the rete mucosum, and it is deposited in the form of yellowish-brown granules.

There are many causes for undue pigmentation of the skin. Those commonly recognized are exposure to the air and the rays of the sun. These affect chiefly persons of dark complexion. Life in the open air with free exposure to all vicissitudes of weather, such as is led by gypsies, tramps, and vagabonds, will induce this, and the covered parts of the body are also affected in such persons owing to long-continued irritation from dirt and varieties of vermin. Dr. Greenhow directed attention to this condition, and named it "vagabond's disease," and showed how it might simulate Addison's disease.[5]

The pigmentation met with on the limbs in stokers and women may also suggest a true melasma. It is, however, commonly reticulated in appearance, and is due to exposure to fire. Dr. Pavy had under his care a case of Addison's disease in a woman in which the pigmentation assumed this form. Phthiriasis of long-standing may induce great deposition of pigment over the body, the face, however, escaping in such a case.

Chloasma uterinum is a well-recognized pigmentary disorder in

gravid women, and may suggest an adrenal melasma. It affects the forehead, linea alba, and nipples more particularly, and passes off with the cause that induced it. The melasma of chronic uterine disease is of the same nature. Tubercular affections of the abdomen are very apt to determine melasma, and it has been noted in connection with hepatic cirrhosis and cancer of the stomach. It is only necessary to enumerate these conditions to place observers on their guard in determining the true nature of melasma in any given case.

It is not without interest, however, to note that in several of the conditions above mentioned the primary irritation or pigmentary excitant has its seat within the abdominal cavity, and we may note, further, in this connection the occurrence at times of darkening of the skin in chronic dysentery and in malarial poisoning, while the same condition may sometimes occur in cases of chronic pulmonary tuberculosis in which tubercles are ultimately developed in the intestines.

Syphilitic eruptions may often leave behind them permanent pigmentation, and that has sometimes led to unfounded suspicion of supra-renal melasma.

The occurrence of patches of parasitic pityriasis (tinea versicolor) in characteristic (covered) situations on the body could hardly be mistaken by any well-trained physician for the melasma now under consideration.

Attention must be directed to pigmentation due to long-continued dosage with arsenical preparations. It is curious how long this condition remained unobserved by physicians, and it is only within recent times that the fact of arsenical melasma has been certainly determined.

In cases of psoriasis, Hodgkin's disease, or of chorea, for example, that have been vigorously treated with arsenic, it is not uncommon to find the occurrence of bronzing and stains on the limbs and body.

This condition might well be mistaken at times for adrenal melasma. It appears gradually to pass away after the drug has been withheld.

Variations in the depth of pigmentation in the course of a case of Addison's disease have been noted, so that the patient is sometimes darker and sometimes lighter.

The hair appears to undergo a deepening of hue, and sometimes becomes like that of dark races.

It must be noted that Addison's disease has frequently been met with where no melasma has ever been present.

Duration of the Disease.—No definite or uniform course has been observed. It is always difficult to determine the exact date of the on-

set of the malady, because the early symptoms may be slight and unnoticed. The fact that exacerbations of the symptoms occur, with remissions leading to renewal of vital powers, has been already noted. There are acute and chronic varieties of the disorder. Many cases end fatally in about eighteen months, others have been observed to last for some years, and in one instance the disorder ran a course of seven years, no doubt illustrating the paroxysmal character from time to time.

Condition of the Urine.—There is nothing specially noteworthy to be recorded respecting the urine in Addison's disease. Careful analyses have been made, and deficiency in the output of uric acid and urea has been generally observed. This is probably the result of diminished waste of tissue, which is the rule in this disorder. An excess of indican (urohæmatoporphyrin) has been rather frequently noted, but it is characteristic generally of some digestive disturbance, or of nervous exhaustion. It may be significant of adrenal disease owing to failure in blood-metabolism, and Dr. MacMunn is strongly of this opinion.

Condition of Other Organs of the Body.—Tuberculosis is probably the most commonly associated morbid state, and nodules of cheesy or cretaceous matter, and groups of tubercles, may be found in the lungs or widely spread throughout the body. Tubercular disease of the spinal column, leading to abscess, is far from infrequent, and stands in definite relation to disease of the adrenals by reason of contiguity. Injuries to the spine have often been noted as the first link in the chain of events leading up to Addison's disease. Spinal caries appears somewhat frequently to precede the disease.

The order of events in this case may not improbably be as follows: As a result of injury, the spinal column is wrenched or damaged. Such mischief is more or less readily repaired and recovered from in healthy subjects. In so-called strumous persons, to whom a special vulnerability attaches, a low form of inflammatory process is set up, more particularly in the bodies of one or more vertebræ, leading to abscess. Bruising of vulnerable parts is now recognized as a condition which renders them liable to infection by such germs or bacilli as may find access to them. In this way a tubercular process may conceivably be established, and this tends to spread, involving in due course the adrenal bodies.

Mammillation of the stomach has been noted with some frequency, also ecchymoses and small ulcers. The former are due to overgrowths of lymphoid tissue around the gastric tubules. These probably soften and lead to the formation of small ulcerations. Enlargement of the solitary and agminated glands of the small, and of the solitary glands

of the large intestines has been not infrequently noticed. Addison noted this lesion.

The lympharia adjacent to the adrenals have been often found enlarged, and imbedded in overgrowth of fibrous tissue. The mesenteric and retro-peritoneal glands are frequently enlarged, and sometimes caseous or firm, from overgrowth of stroma and atrophy of glandular structure.

The spleen has been found enlarged, sometimes greatly so, dark, and softened, but with no great frequency. Clinically, splenic enlargement is not commonly detected. Nothing has been noted respecting the condition of the thyroid body. Cerebral softening and sub-arachnoid effusion have been met with, also pericarditis with effusion. These are, however, only occasional and secondary changes, and form no part of the malady as commonly understood.

The liver presents no specially noteworthy changes, and the same may be affirmed in respect of the kidneys.

Without doubt, some of the most important associated morbid changes relate to the condition of the great abdominal nervous plexuses, and we must next direct careful attention to this. We have already seen how direct and intimate are the relations between the adrenals and this part of the nervous system. Careful dissections have repeatedly shown that the ganglia and branches of the abdominal sympathetic nerve are involved in the inflammatory processes which have taken place either primarily in the adrenals themselves, or have reached them by extension from other inflamed (and probably infected) contiguous structures. Such dissections are extremely difficult to execute, requiring, as only those who have attempted them can know, great patience and anatomical knowledge. The semilunar ganglia have been found altered in structure, enlarged and redder than natural. Dense meshes of fibroid tissue have been observed enveloping them and the nerve-branches connected with them. This new growth proceeds from the connective-tissue capsular investment of the adrenals, and gradually invests and mats together the ganglia and delicate nerve-fibrils. The growth is generally very dense and hard, and the difficulty is to determine accurately what is nerve-matter and what is mere fibrous tissue. The supra-renal and solar plexuses thus become fused, as it were, into a matted felt of encroaching and enveloping fibrous overgrowth. The nerve-cells of the semilunar ganglia have been found opaque and granular, with traces of former hemorrhages into their structure. Branches of nerves proceeding to the adrenals from these ganglia have been seen enlarged, and in one instance Dr. Cayley found a branch of the great splanchnic nerve at least twice the size of a healthy nerve. This enlargement was due to

increased fibrous growth in the nerve-sheath. In Dr. Tuckwell's dissection, which is now in the Museum of St. Bartholomew's Hospital,[6] it is seen that fibrous overgrowth caused matting of all the nervous plexuses, and this extended up the splanchnic and pneumogastric nerves, and became continuous with firm old adhesions which surrounded the liver and spleen, and bound the upper half of the omentum to the anterior abdominal wall. No change was found microscopically in the nerve-fibres proper, but the nerves have been noted as small in one case (Professor Tigri). We are thus in face of a proliferating connective-tissue fibrosis, spreading over parts immediately contiguous to the adrenals, and part of this process must be regarded as entailing greater or lesser degrees of both neuritis and perineuritis.

To appreciate the full significance and gravity of such a process, it is only necessary to realize the complex and widely radiating relation of the great epigastric or solar plexus. It supplies all the abdominal viscera. It receives the great splanchnic nerve on both sides of the body, part of the lesser splanchnics and the termination of the right pneumogastric nerve. Its semilunar ganglia are the largest in the body, and they lie close to the adrenal glands. Ten different nervous plexuses issue from the solar plexus. One of them, the adrenal plexus, is formed by branches from the solar plexus, from the semilunar ganglia, and from the splanchnic and phrenic nerves, a ganglion being situated at the junction of the latter nerve. This plexus is remarkable for its large size in relation to the smallness of the organ it ministers to. The other plexuses are the phrenic, cœliac, gastric, hepatic, splenic, renal, superior mesenteric, spermatic, and inferior mesenteric. We may now comprehend the magnitude of the interference with due performance of nervous function which is necessarily entailed by the fibro-sclerosing process already described, and find explanation therefrom for many of the specific features and symptoms pertaining to Addison's disease. So markedly is this the case, that some observers regard the essential nature of the malady as depending rather on the nerve-changes entailed by the disease of the adrenals than on the specific lesion in those organs. It is at all events certain that some examples of Addison's disease have been met with in which no primary changes were observable in the adrenal bodies, but solely in the semilunar ganglia.

This brings us face to face with the conflicting theories that have been advanced respecting the etiology of the disease, and these must now receive attention. Much difficulty has arisen from the fact that aberrant forms of Addison's disease have been met with. Addison believed that the train of symptoms he described would ensue in any form of destructive lesion which involved the adrenals, and in his me-

moir he gives the particulars of four cases in which these organs were destroyed by cancer. At a later period, his pupil Dr. Wilks pointed out that in these cases the true symptoms of Addison's disease were not really present, and it is now generally recognized that cancer of the adrenals does not produce this disease. We are therefore confronted with the strange fact that mere destruction of the adrenals is not in itself a necessary cause of true Addison's disease. The doctrine of Guy's Hospital School has generally supported the view that the destructive changes are practically specific in this disease, and are of the nature already described. In other words, the lesion is a tubercular one.

There is sufficient evidence now to prove that the adrenals may be gravely diseased without inducing Addison's disease. Death may ensue from other causes or complications such as phthisis or nephritis before melasma sets in. As will be shown later, malignant growths may occur in the adrenals of primary or of secondary character, sometimes of large size, and death ensues without the characteristic concomitants of Addison's disease. In such instances, we may fairly believe that the processes are too rapid to lead to the involvement of the adjacent nervous structures in the manner characteristic of progressive and sclerosing tuberculosis. In this connection it was noted by Moxon that even large cancerous growths in the liver often fail to set up jaundice.

Further difficulties, however, await us, and we have to account for cases in which melasma occurs, as a leading symptom, without any obvious disease of the adrenals. We have already discussed the varieties of melasma which may often simulate the specific adrenal form, and it is quite certain that many of the examples brought forward in support of the view now under consideration may be safely relegated to other categories of pigmentation.

By far the most important class of cases to excite doubt as to the special nature of Addison's disease is that in which obvious symptoms of the malady occur, leading to death, and in which no gross changes are found in the adrenals, but instead atrophy, sometimes to the most extreme degree, is discovered. Some of the most careful and competent pathologists are agreed upon these facts, and they must be accepted and reckoned with (Coupland).[7] I am myself well satisfied on the point. The adrenals may thus be most difficult of detection in making an autopsy, and entire absence of any remaining structure has been noted. Small thin masses or relics of the gland may be found, little more than collections of pigmented granules, or organs shrunk to one third or less of their natural size and weight. Both glands may be absent in cases of this nature. We have no

knowledge whatever respecting the occurrence of congenital absence of one or other of the adrenals. We have already pointed out that a gland may exist in its proper situation in cases of congenital absence of one kidney. But in the cases now before us we have to deal with a definite train of symptoms sufficiently recognized as indicating Addison's disease as a whole, in which, during life, we decide that the adrenals are unquestionably involved. Death occurs, and we expect to find, almost certainly, that the adrenals are the seat of gross lesions and enlargement. On the contrary, we find atrophic conditions more or less pronounced. In most of the recorded cases illustrating the latter condition, there have been found associated changes in the adjacent nervous ganglia and sympathetic fibrils. This fact is of prime importance in the case, and we are at once led to inquire whether these remarkable trophic changes in the adrenals may not be the result of primary disease in these nervous structures so remarkably associated with the glands in question. This is Dr. Coupland's interpretation of the difficulty. He thus conceives that the adrenals waste under the same influences that evolve the symptoms and the fatal cause of the malady.

If this view be accepted, we must necessarily drop the belief that Addison's disease is uniformly the result of a specific lesion in the adrenals, as has been long taught in the Guy's Hospital School, and we must enlarge our conception of the etiology of the disease.

Our present knowledge forbids the acceptance of the simple unity of Addison's disease, and the fact that gross changes in the abdominal sympathetic system, without implication of the adrenals, have been observed lends additional support to the larger and more comprehensive view of the pathology of this condition.

A case reported by Dr. Hadden [8] is noteworthy in this connection. He found the adrenals destroyed by a fibroid process or cirrhosis in one example of Addison's disease, and the semilunar ganglion infiltrated with similar fibro-nuclear growths. He believed that the sympathetic fibres were necessarily much involved in the process.

It has been sought to explain the occurrence of atrophy of one or both of the adrenals by supposing that the wasting is the ultimate stage of the more commonly recognized enlarged condition. I am not prepared to accept this view. If we regard the most frequent lesion of the adrenals in Addison's disease as one of a tubercular nature, we are hardly warranted in expecting atrophy as the ultimate outcome of such a process in any case. This is not the experience of the dead-house in other examples of tubercular processes. They are apt to leave readily recognizable changes behind them, gross indeed, even if obsolescent.

Dr. Saundby, of Birmingham, has recently suggested, as did Dr. Duclos, of Tours, that the general symptoms of Addison's disease are explicable on the view that some poison is generated in the blood, possibly the result of some imperfect pigmentary metamorphosis. At the present time, we can only state that if this be the case we have no certain knowledge of such peccant material, and it must remain for future researches to bring it to light.

The question of any microbic elements capable of generating a specific poison must not be left out of consideration, although there are no facts to justify any opinions on the matter. The existence of the tubercular bacillus is sufficiently proved as the most certain and frequent exciting cause of the primary lesion of the adrenals in Addison's disease. The remarkable fact remains that in cases of general tuberculosis these organs appear to be little if at all involved, and are certainly not to be reckoned amongst the most vulnerable tissues for invasion by the bacilli of tubercle.

The fact that the symptomatology of Addison's disease may vary materially in different cases in respect of nervous symptoms and of the presence or absence of melasma has been pointed out, suggestively, by Dr. Bedford Fenwick, and will again be alluded to. He is of opinion that cortical disease primarily and mainly involving the adrenal bodies entails melasma, while medullary disease gives rise to graver and more prominent nervous symptoms. The anatomical and physiological relations of the two parts of these organs appear to warrant this conception.

It is certain that, as has been already indicated, acute cases, of rapidly fatal ending, are often devoid of pigmentary symptoms.

Further investigations in this direction appear to be necessary, but we may believe that this distinction is rather too fine, and that gross disease in the cortical portion will very soon involve the medullary district, and *vice versa*.

There can be little doubt that a large part of the symptomatology of Addison's disease depends upon the morbid condition of the abdominal nerve-centres. Many well-known facts come in to support this belief. The occurrence of nausea, gastric crises, vomiting, depressed circulation, collapse, and sinking sensations are all consonant with the idea that these sympathetic centres and nerve-fibres are gravely involved. We have already enumerated their wide-spread connections, and shown how far-reaching may be the morbid radiations from them. We have further noted the occurrence of pigmentary changes in connection with chronic irritation of various abdominal organs innervated from the same source, and we have also seen that there is strong reason for believing that the adrenals in particu-

lar have to do with a very special variety of pigmentary metabolism in the system. We have also to bear in mind not only the proximity of these great vital nerve-centres to the adrenals, but the fact that these organs have an inordinate nervous supply among their intimate tissues far exceeding that of any other viscera in the body. If many of the symptoms are due to what Dr. Goodhart terms "strangling of the abdominal sympathetic," we not seldom find causes at work to induce this both in Addison's disease and in some other morbid conditions, such as Hodgkin's disease, chronic inflammation of lymph-glands, and scirrhous cancer, and such examples have been sometimes recognized clinically, and determined after death.

Treatment.—It has to be confessed that with increase in our knowledge both of the nature and symptoms of this malady no corresponding improvement has been made in respect of its treatment.

Having regard to the lowered vitality and impaired health which form the special features of the disorder, efforts have always been made to raise the level of nutrition, and place the patient in the most favorable condition to attain the highest general health possible.

In addition to this, the various urgent symptoms have been met as they arose.

The main line of treatment indicated by a consideration of the primary pathological process in the adrenal bodies is that proper for tuberculosis in any part of the body. Hence, removal from urban environment to pure country air and wholesome dwelling-places is imperative. The patient is little capable of attending to his duties, whether domestic or of a business nature. Asthenia is the key-note of the malady. Generous diet, containing all nutritive elements in abundance, is desirable, and some good wine should be given. All varieties of fresh meat and fish, also oysters, with well-cooked vegetable food, fat, cream and milk, and farinaceous food are allowable.

When gastric irritability is present, the diet must be altered, and treatment as for nervous vomiting be adopted. Recumbency is necessary, not seldom, both for this symptom and for the cardiac debility which is commonly associated with it. Milk and lime-water, one part of the latter to two parts of the former, given in teaspoonful doses at intervals of a quarter of an hour, by the clock, will often be borne by very irritable stomachs. Larger quantities may be rejected. Whey is useful, and kumyss may be available. No solid food is permissible. Valentin's beef-essence, given with iced water in small quantities, may be borne. Sometimes it is well to cease feeding altogether by the mouth, and to resort to rectal alimentation by nutrient enemata or suppositories. A day or two of complete rest to the stomach may thus be secured, and subsequently simple food may be naturally

retained. Alcohol in some form is generally necessary, and brandy with aerated water or champagne diluted with the latter or with iced water may be well borne, and some brandy may also be put into the nutrient enemata. Sinapisms to the epigastrium are useful for the vomiting, and various medicines are available for this troublesome symptom. Tartrate of sodium in effervescence with a few minims of dilute hydrocyanic acid is often serviceable, or a small pill containing one-fourth of a grain of morphine and a minim of creasote may be given. Hypodermic injections of a sixth of a grain of morphine with one-hundredth of a grain of atropine may be employed.

Recurrent paroxysms of gastric irritability and of cardiac asthenia form part of the history of many cases of Addison's disease, and as these pass off under rest and suitable treatment the patient may improve materially in all respects for weeks or months. The cases vary in degree and in acuteness, as has been already noted.

It has been proposed to apply counter-irritation to the loins by means of liniment of iodine, with a view to treat the chronic inflammatory processes in the adrenals and the adjacent nervous plexuses, but not much benefit can be expected from such a course.

There is no special indication for treatment derivable from the theory that many of the morbid conditions are due to the circulation in the system of toxines, produced by the imperfect pigmentary metabolism which is necessitated by disease of the adrenals.

A new era in therapeutics has certainly dawned since the discovery that the ravages of myxœdema may be checked and almost, if not quite, abolished by supplying to the system the material of the thyroid body which is cut off owing to the morbid condition of the gland in that malady, and it has been surmised that we may do good in Addison's disease by grafting adrenal tissue into some part of the body, or by employing an extract from the adrenal bodies of the sheep in a manner similar to that practised in cases of myxœdema.

By the kindness of Dr. George Oliver, of Harrogate, I am permitted to refer to some very important experiments which he has recently made in the Physiological Laboratory of University College (London) with Professor Schäfer, and which are still unpublished. An extract of the adrenal bodies, in the form of a tincture, was made by Messrs. Willows, Francis, and Butler, of which one minim is equal to one grain of the gland, and this was injected into the veins of dogs.

A dose equivalent to three grains produced, first, a remarkable increase of blood-pressure, double or treble that recorded before the injection; secondly, powerful contraction of the arteries as shown by the plethismograph applied to the limbs, the oncograph enclosing

the kidney, and the arteriometer applied to the bared femoral artery —this effect, taking place even though the spinal cord and the brachial plexus were cut, was apparently of peripheral origin; thirdly, stimulation of the vagus; and fourthly, stimulation of the cardiac muscle.

Dr. Oliver finds that the properties of the extract are not impaired by boiling, and they are not due to the proteid elements or to neurin (as has been conjectured), but probably arise from the presence of an alkaloidal body. Alcohol, whether absolute or rectified spirit, extracts the active principle.

He considers that this preparation may be found of service in Addison's disease, and also in cases of exophthalmic goitre.

Dr. Oliver had previously found that this extract given by the mouth in the human subject contracted the calibre of the radial artery (using his arteriometer), and this led him to further experiments on dogs, cats, and rabbits with uniformly similar results.[9] The active agent he believes to be alkaloidal in its nature, and, as it will not dialyze, its molecule is probably very large.

Sir T. Grainger Stewart, of Edinburgh, has employed feeding with adrenal bodies in one case of Addison's disease, but without benefit.

For general tonic purposes no better remedy is known than iron, and this is best combined with strychnine and arsenic.

The tincture of perchloride of iron in ten- or fifteen-minim doses, with four or five of the liquor strychninæ hydrochloratis, and three or four of the liquor arsenici hydrochloricus,* given with glycerin, forms one of the best remedies I know of. Cod-liver oil and extract of malt are sometimes useful, but Dr. Greenhow found glycerin of more value in doses of one or two drachms.

Strong purgatives are to be carefully avoided at all times in the treatment.

Over-fatigue is especially to be guarded against.

For nausea, retching, hiccup, and qualms, I would suggest the employment of nitro-glycerin, in doses of one or two minims of the liquor trinitrinæ, or it may be given in small tablets in equivalent doses of $\frac{1}{100}$ grain, repeated every three or four hours.

Prognosis.—We have so far no certain evidence of the complete arrest or cure of any case of this malady. Temporary improvement is all that can be looked for. Some of the chronic cases appear to last for five or six years. The average age at death is from thirty to thirty-five.

It is interesting to note that Addison's disease is rarely met with

* Preparations officinal in the B. P., containing each about one per cent. of the active agent.

in the upper classes of society. Dr. Greenhow found that nine-tenths of the cases occurred in the laboring classes. The mortality is almost entirely distributed over the laborious period of life, and males suffer much more than females.

These facts are held to indicate that injuries, strains, and falls have more to do with inducing the malady than is commonly believed, and the inability of the laboring classes to rest sufficiently and recover soundly from such injuries may be also taken into consideration. The majority of cases in females occur in hard-working servants and poor married women. The following conclusions have been arrived at by Dr. Bedford Fenwick,[10] from an analysis of thirty cases recorded in the Pathological Society's Transactions, London, from 1866 to 1880:

That cases without melasma usually die early, within five months, those with bronzing within two years from the first onset of symptoms; that bronzing may be due to degeneration of the cortical layer, and the constitutional symptoms to implication of the medullary portion, and that if the latter be mainly diseased or first involved the constitutional symptoms may be rapidly developed and death occur before melasma takes place; that if bronzing exists both adrenals are almost invariably involved, but that in a distinct proportion of cases without melasma only one organ, and that generally the right, is affected. We have already discussed the conclusions just mentioned in respect of disease involving the cortex or medulla primarily.

OTHER DISEASES OF THE SUPRA-RENAL CAPSULE.

Atrophy.

Allusion has already been made to this condition as met with in certain cases of Addison's disease where the ordinary symptoms of that disorder have been present.

Atrophy is not a common morbid condition. A few instances have been noted in which one adrenal body was greatly atrophied, and the corresponding organ could not be found. Some degree of wasting occurs as a senile change.

There may be simple atrophy, and atrophy as an apparent result of chronic interstitial inflammation akin to that met with in the kidney or liver. Atrophy may be discovered after death when no symptoms during life have pointed to such change. The only recognized symptoms have been those of Addison's disease, as already mentioned. Sir William Broadbent has recorded a case where the adrenal was exceedingly small, and the kidneys were extremely shrunken

and granular. The adrenal corresponding to the smaller kidney, which was only three-quarters of an inch in length, preserved its form. The woman from whom these organs were taken died of uræmia. The organs were presumably congenitally small.[11] One of the most remarkable instances was that recorded by Dr. Wickham Legg,[12] where, in a case of Addison's disease, no right adrenal was found, and extreme fibrous degeneration of the left was present. I was present at this autopsy, and Mr. Luther Holden assisted at it. The left organ was a mere shell or fibrous capsule and contained nothing. Fibrous tissue and pigmented fat were all that could be detected in the wall of this adrenal body. Cases have also been well described by Dr. Goodhart[13] and Dr. Davy of Exeter[14] in which Addison's disease occurred with marked atrophy of the adrenals.

Hemorrhage into the Adrenals.

This is due sometimes to injury, and sometimes to an acute inflammation. Convulsive attacks may induce it, as in a case of a child aged seven months in which paroxysms of whooping-cough were the apparent exciting cause of extensive hemorrhage into each adrenal body. (Specimen preserved in Saint Bartholomew's Hospital Museum.) An appearance of hemorrhage is sometimes caused by mere decomposition in the organs, the medulla breaking down into a cavity containing dark grumous fluid. Apoplexy of the adrenals has been several times met with in males.

Amyloid or Lardaceous Degeneration.

This may occur in cases where this deposit is largely disseminated. I have observed it in several instances associated with renal, hepatic, and intestinal lardaceous changes. Thus, it may occur in phthisis, syphilis, and in cases of long-standing suppuration (depuration disease—Dickinson). As is now well known, with the advance in modern surgery, lardaceous degeneration is more and more rarely met with than was formerly the case. The change occurs chiefly in the small arteries, and is brought to light by the application of solution of iodine.

Abscess.

This is occasionally found, due to septic infection from some other and possibly distant part of the body. Caseous material may sometimes, but not frequently, break down into pus. In one case, that of a man, aged sixty-seven, who died of diabetes, the adrenal was converted into a globular mass three inches in circumference. The gland was destroyed and the walls were thickened by deposit of caseous mate-

rial. The cavity was full of sanious pus. The other adrenal body was healthy. There were no symptoms of Addison's disease during life. (Specimen in Museum of St. Bartholomew's Hospital.)

Cysts.

These may be met with, but are rare. A case is described[15] of a man, aged sixty-one, who died a few days after a severe injury to his spine, and in the left adrenal body a cyst the size of a boy's marble was found, having almost transparent parietes, and containing tinted serum. The remaining part of the organ was healthy. Colloid matter may be found in adrenal cysts. Hydatid cysts have been met with. No symptoms attach to these.

Fatty Degeneration.

This is not very uncommon, and appears to be most frequently observed in elderly persons. No associated symptoms have been noted.

My colleague, Dr. Kanthack, Lecturer on Pathology at St. Bartholomew's Hospital, has kindly furnished me with some of his unpublished researches into the condition of the adrenal bodies in respect of the presence or absence of fatty matter, more especially in the cortical portions. He states that it is affirmed that the cortex of the adrenal bodies in adults is fatty. Dr. Kanthack finds that fatty degeneration is met with in cardiac diseases, in pulmonary diseases, and in anæmia. At birth, it is stated that no fat is found in the capsules, that gradually the cortex becomes lighter and eventually yellow, owing to the presence of fatty matter. In emaciation, the fat is said to disappear. Dr. Kanthack* finds that most healthy children show very little fat in the capsules. Newly born kittens always show much fat in the liver and adrenals, and this condition lasts for three or four weeks, even when the animals are well-fed. He has not yet examined young animals at later dates. In starving, marasmic infants (a few months old) the cortex of the adrenals is very fatty. Still-born, or very young, infants show hardly any fat, but these are exceptional cases. Starving of animals for from thirty-six to sixty hours causes a marked appearance of fat in the capsules, or at any rate of a great increase in previously existing fat. In these cases of starving, the fatty changes in the adrenal bodies are always in advance of those met with in the liver, and not seldom the latter organ is quite free from fat.

Acute and subacute poisoning (bacterial, snake, mineral, *e.g.*, tartarated copper) causes a marked fatty degeneration in the capsules, large droplets of fat appearing.

* Experiments conducted with Mr. Atlee.

Fatigue (experimental), *e.g.*, running an animal till it drops, produces the same changes.

It would appear that conditions and symptoms associated with fatigue, asthenia, or marasmus are accompanied by striking degenerative changes in the adrenal bodies, and that these changes often appear early, before they occur in the liver and kidneys.

Dr. Kanthack believes that it follows from Schäfer's, and Oliver's experiments that the adrenal bodies contain a tonic substance. With progressive fatty degeneration this substance must cease to be formed, and thus marantic symptoms are apt to arise in any case in which this occurs.

These interesting experiments appears to me to open up some very suggestive lines of thought, and to indicate that further researches in the same direction will be likely to prove fruitful.

Embolism.

Embolism of the capsular arteries has been met with, and is probably always associated with embolic processes in other arterial tracts of the body.

Carcinoma and Sarcoma.

Carcinoma may be primary in the adrenal bodies, but is more commonly secondary to such growth in neighboring structures. In 123 cases of new growths (102 carcinoma, 21 sarcoma), Dr. Norman Moore found secondary growths in the supra-renal capsules in only 8. Of these, 2 occurred primarily in the lungs (sarcoma), 2 in the heart (endothelioma), 1 in the brain (sarcoma), 1 in the kidney (carcinoma), 1 in the stomach (carcinoma), 1 in the œsophagus (carcinoma). Microscopic examinations were made in each case.[16] In these cases it is usual to find new growths widely disseminated over the viscera. Round-celled sarcoma appears to be the commonest form met with. Dr. Pye-Smith has recorded a case in which primary sarcoma occurred in each adrenal body in a child. Direct extension of malignant growths may be met with where the disease has spread from the kidney, lumbar glands, vertebræ, or pancreas.

Addison, in his memoir, included four cases of cancer of the adrenals, and he believed at first that any disease which entirely destroyed these bodies could produce the characteristic symptoms of the disorder he described. Dr. Wilks proved that this was not the case, and that cancer of the adrenals was incapable of producing true Addison's disease. There may be a tumor of the capsules so large as to be palpable during life, but this is an extremely rare event. It is very noteworthy that disease so completely destructive of these or-

gans should fail to induce the characteristic symptoms of Addison's disease. An explanation of this fact is suggested by analogy with cancerous growths in the liver, which often fail to set up jaundice and other symptoms, all of which might naturally be looked for in such cases. The process is often so rapid and acute, and so frequently fails to strangle the nervous structures adjacent to those organs, that there is hardly time for the induction of many of the leading symptoms of Addison's disease.

The fact remains that in the majority of cases of malignant disease of the adrenal bodies, the condition of these organs is not clinically recognized and is only discovered at the necropsy. Other features of the case are more prominent and obvious. Nine cases of cancer have, however, been recorded in which bronzing of the skin occurred without other specific symptoms of Addison's disease.

The duration of these cases is generally not more than a year. In one instance, an adult was treated for dyspepsia for two years, and subsequently developed symptoms like those of phthisis. He was deeply jaundiced and delirious during the last two weeks of his life. There was found cancer of the head of the pancreas, the lungs and kidneys were full of cancerous masses, and the right adrenal body was infiltrated with carcinoma. In not a few of these cases, the age of the patient is more advanced than that at which Addison's disease is most apt to occur.

Tuberculosis.

This is without doubt the most frequent and important of all the diseases affecting the adrenal bodies. We have here to deal with that special affinity which has so long been surmised to exit between Addison's disease and the scrofulous diathesis or habit of body. No morbid condition of the adrenals is so common as this, and the latest researches point, as has been already shown, to the fact that the characteristic lesion of Addison's disease in the adrenal bodies is bacillary tuberculosis in varying degrees and stages.

Tuberculosis occurs in three forms.

1. *Gray or Miliary Deposits.*—The adrenals may be wholly destroyed by these. There may be no tubercular deposits elsewhere in the body, but most commonly there are others in the lungs, bronchial and mesenteric glands. Melasma is usually associated together with other symptoms of Addison's disease.

2. *Larger Caseating Masses.*—These may wholly, or almost wholly, replace the natural tissues of the glands. Translucent grayish material may often be associated with caseous masses. In this condition, there are usually deposits of tubercle in the lungs.

3. *Calcareous Concretions.*—These may be hard, almost horny in consistence, and gritty, grating on section. This condition and the preceding are in fact characteristic of chronic tuberculosis in any organ, and especially of pulmonary tuberculosis. They may be regarded as indicating adrenal phthisis, and tubercle bacilli are almost always to be recognized if carefully sought for. Adrenal tuberculosis may be, and often is, primary, but it is more often secondary to other deposits.

While constituting the special lesion of the adrenals in true Addison's disease, it would appear that caseous masses may be deposited in the adrenals without the occurrence of the ordinary symptoms of that malady. Thus Dr. Pye-Smith has given me notes of a recent case of pulmonary and laryngeal phthisis, with alcoholic cirrhosis of the liver and ascites, in which in one adrenal body there was an opaque caseous mass the size of two peas, and in the other body two smaller similar masses. The natural tissue was pushed aside, but not otherwise affected. There was no softening or contraction, and no thickening of the surrounding connective tissue. During life there were no symptoms of Addison's disease.

As has been already pointed out, chronicity of the tubercular process is an important factor in determining most of the characteristic symptoms, and the condition of fibrosis with entangling adhesions to adjacent parts appears further to be a very constant requirement for their due development in any case.

Hyperplasia.

Circumscribed hyperplasia of both glands has been met with, the cortex being alone affected.[17] On examination these growths were found to be well defined, and separated from the rest of the organ by a fibrous capsule. The cortical substance was overgrown, and there were fatty infiltrations and degeneration of the tubal cells. The tubes were enlarged, the stroma thickened, and the capillaries dilated. No symptoms during life indicated any such changes. A case of hyperplastic tumor in a male fifty-two years of age is recorded by Seitz.[18]

It may fairly be affirmed that but little clinical interest attaches to any but the changes induced in the adrenal bodies by tubercular and malignant growths and by atrophic processes. With the advance of knowledge, which is constant, we may not improbably come, in due time, to recognize the clinical symptoms which are specifically significant of many other of the gross diseases of the adrenals, and we may even look forward to the possibility of recognizing some of the functional abnormalities of these organs.

Supernumerary Adrenal Bodies.

A remarkable instance in which four adrenal bodies were met with was lately recorded by Dr. Newton Pitt, of Guy's Hospital.[20] Two were found in the normal position. Beneath the capsule on the anterior surface of the kidneys, which were healthy, were two additional glands whose structure was normal. They lay about an inch from the upper end of the kidney.

Supplementary adrenal bodies are generally small, but large ones have been found.

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DIABETES MELLITUS.

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DIABETES MELLITUS.

INTRODUCTION.

Definition.—By the term Diabetes Mellitus is understood a disease characterized by an excretion of grape sugar in the urine, continued through weeks, months, or years, following the ingestion of moderate amounts of carbohydrates, or even, in certain cases, when no carbohydrates have been taken into the system.

This definition calls for certain amplifications:

a. The excretion of grape sugar (glycosuria) must have continued for a certain length of time to justify the nosological term "diabetes mellitus," for a temporary glycosuria of a few hours' or days' duration may follow any one of a number of insults to the organism, such, for example, as that from nervous irritants or from the introduction of certain poisons; and such an evanescent excretion of sugar in the urine affords no justification for the diagnosis of diabetes mellitus. It is often difficult to draw the dividing line between this symptomatic glycosuria and true diabetes mellitus, and in such cases the duration of the glycosuria is of weighty diagnostic significance.

b. In order to justify the designation diabetes mellitus, the excretion of sugar in the urine must take place after the ingestion of *moderate* amounts of carbohydrates, for a glycosuria appearing after the taking of excessive quantities of carbohydrates is not a pathological symptom (see below).

c. It is better to restrict the term diabetes mellitus to those cases in which the sugar excreted is grape sugar. Isolated cases, indeed, are on record in which other forms of sugar, especially fruit sugar (levulose), have been found in the urine, but these instances are so rare and as yet so unexplained that we are obliged in practice to ignore them.

d. The definition which I have given is, strictly speaking, a very superficial one. It seizes upon only one feature of the morbid complex and ignores the other clinical symptoms, the polyuria, the polydipsia, the polyphagia, the emaciation. But the definition cannot be justly criticised on this account, for all these and other clinical

symptoms are of secondary importance, they are in a measure dependent upon the glycosuria, and are often absent. A more serious objection would be that a definition should not rest upon the symptoms at all but should refer rather to the nature of the disease. But in the case of diabetes mellitus we are in the difficult position that we are ignorant of the nature of the disease, and any attempt at a more exact definition would at once involve a contradiction at one point or another.

For example, I am strongly inclined to define the disease in the following formula: *By the term diabetes mellitus is understood a disease in which the capacity of the organism for burning up grape sugar is morbidly depressed.* We shall, indeed, see that all the phenomena of diabetes may, without compulsion, be explained by this formula, yet I hesitate to place the definition at the head of this treatise for the reason that we have as yet no certain evidence that it exhaustively explains the condition actually present.

History.

But few words need be said here concerning the history of the disease. Diabetes was apparently known to the oldest medical writers, for unmistakable references to the disease are found in the writings of ancient Indian physicians and also in the works of the Roman Celsus and of the Greek Aretæus (both in the first century after Christ). They speak of an affection which is accompanied by the passage (διαβαίνειν, to pass through) of enormous amounts of urine, unquenchable thirst, and emaciation. From that time the disease was frequently treated of in the writings of the ancients, but no more definite description of the affection was given.

The discovery of sugar in the urine of diabetics was first made in the seventeenth century by Thomas Willis, an Englishman, and rested upon the appreciation of a sweet taste in the urine. Another Englishman, M. Dobson (1775), was the first who actually obtained sugar from the urine. After this characteristic symptom became generally known, many celebrated physicians in later periods rendered valuable service in their descriptions of the disease. Among those most deserving of mention in this connection I would name John Rollo and W. Prout in England, and Bouchardat and Mialhe in France.

Definite scientific investigations into the causes and nature of the disease were first begun, however, about the middle of the present century. They date from the celebrated experiments of Claude Bernard, which are well known to every investigator under the name of sugar-puncture (*piqûre, Zuckerstich*). Since that time the literature

of diabetes has grown to enormous dimensions, and in the study of no disease have more experiments upon man and animals been made. The names which stand out most prominently in connection with the development of our knowledge, both theoretical and practical, of this disorder are the following: Claude Bernard, Bouchardat, Brücke, Cantani, Dickinson, Ebstein, Frerichs, F. A. Hoffmann, Külz, Lécorché, von Mering, Minkowski, Naunyn, Pavy, Seegen, and C. von Voit.

PHYSIOLOGY AND GENERAL PATHOLOGY OF SUGAR EXCRETION.

I. The Carbohydrates of Food and Their Absorption.[1]

In order to gain a clear idea of the ultimate fate of the carbohydrates in the body we shall do well to begin with those of the food.

Starch.—The most important alimentary carbohydrate is starch (amylum). This is a material which is compounded of several smaller carbohydrate molecules, and which is for this reason called polysaccharid. Starch cannot be absorbed as such, and must first be decomposed by a process of fermentation into the easily soluble carbohydrates. This decomposition is a process of division in which several smaller carbohydrate molecules (monosaccharids and disaccharids) are formed from the large carbohydrate molecule (polysaccharid). The polysaccharid *glycogen* has to undergo a similar conversion before it can be absorbed.

The ferment (*diastase*) through the action of which this division is accomplished is found more especially in the buccal secretions and in the pancreatic juice, but it seems to be entirely wanting nowhere in the body.

Diastase gives rise to the formation from starch of the following bodies, some of which are produced consecutively, others simultaneously, viz., soluble starch (amidulin), erythrodextrin, achroödextrin, isomaltose, and maltose. As these division-products of starch pass into the intestinal wall and portal vein they undergo a further change, being almost entirely converted into grape sugar (glycose, glucose, or dextrose). Dextrin and maltose meet, of course, the same fate when taken as such in food or drink.

Cane sugar (saccharose) is a disaccharid; it is split up in the alimentary canal, through the action of acids, ferments, and bacteria, into its two components, grape sugar and fruit sugar (levulose), and in this shape is absorbed. It is only when cane sugar has been ingested in very large quantity that any of it passes unconverted into the blood.

Fruit sugar (levulose, present in ripe fruits and in honey) is taken into the blood unchanged.

Milk sugar (lactose) also passes unchanged into the blood.

Cellulose is probably never absorbed, although a portion of it is lost in the intestinal canal, it being very easily fermented and changed by the action of the bacteria into methan, carbonic acid, acetic acid, and butyric acid.

From the intestinal wall the carbohydrate stream flows through the portal vein to the liver. According to the nature of the food ingested various forms of carbohydrates take part in this procession—glucose, levulose, lactose, saccharose, and traces of dextrin and maltose. It is furthermore evident that the richness of the portal blood in carbohydrates must be very variable. While in fasting or flesh-and-fat-fed dogs the percentage of carbohydrates in the blood of the portal vein is from 0.10 to 0.15, von Mering found it increased to 0.4 and more after feeding the animals with carbohydrates.

II. The Formation of Glycogen from Carbohydrates.[2]

What now further happens with the carbohydrates? The work of Claude Bernard furnishes an answer to this question. His investigations have been frequently repeated and in the main confirmed. We are indebted to E. Külz and C. von Voit, however, for some amplifications of his teachings.

As long as the quantity of carbohydrates passing from the intestine to the liver remains moderate, it is a matter of no importance as regards their further destiny under what form they enter the liver; the result is the same whether it be grape sugar, fruit sugar, milk sugar, or other kinds, that the portal blood conveys from the intestine to the liver. The liver takes hold of the carbohydrate and converts it into glycogen, which is deposited in the hepatic cells in the form of flakes, and probably in loose combination with albumin (glycogen-fattening of the liver).

The liver is a reservoir for carbohydrates, and is so capacious that it may contain as much as 14 per cent. of its own weight of glycogen.

The existence of this storage-place permits of a regulation of the amount of sugar contained in the blood of the hepatic veins and of the arteries. An examination for sugar of the blood of the hepatic veins and of the arteries in the most various parts of the body has been repeatedly made in healthy animals (and also in healthy men) after the ingestion of carbohydrates and of albumin, and when fasting, and the proportion has always been found to be constant or to vary

between very narrow limits, viz., from 0.12 to 0.18 per cent. The interposition of this glycogen reservoir also acts in such a way that the outflow remains the same, whatever fluctuations there may be in the inflow, and that there is constantly circulating in the arterial blood a saccharine solution of a concentration best adapted to favor the normal course of all the functions. We may say, in short, that the liver watches over and regulates the proportion of sugar contained in the blood leaving it.

We have now several times spoken of the percentage of sugar in the blood of the hepatic veins and of the arteries. What kind of sugar is it? It has been clearly proven that we have here to deal with grape sugar. Of other carbohydrates glycogen alone enters into consideration, but this is met with only in almost infinitesimal quantities. The maximum percentage found by Huppert (in the dog) was only 0.0025.

Glycogen is found, however, in other organs than the liver, especially in the muscles. The quantity contained in the latter varies, being greater after the ingestion of large amounts of carbohydrates and after a long period of rest, than after abstinence from food and after exhausting labor. It has been found that in general the amounts of glycogen contained in the liver and in the muscles increase and decrease along parallel lines, that as a rule the total quantity of glycogen in the liver is about equal to that contained in all the muscles of the body, and finally that, in the case of glycogen impoverishment of the body (see below), the muscles are more tenacious of their store of glycogen than is the liver. The muscles are therefore likewise a glycogen depot.

How does the glycogen reach the muscles? It would appear that the latter elaborate their own store of glycogen from grape sugar. This grape sugar is always at hand for the use of the muscles, for the liver looks out for the maintenance of a certain percentage of grape sugar in the blood. The liver does this while giving up its glycogen. It excretes at the most only traces of this substance unchanged, the greater part of it being first converted into grape sugar. Thus we see that the liver is more than a simple carbohydrate reservoir, it is also endowed with recoining powers. It collects the superfluous carbohydrates from the portal vein, fixes them in a form which is not readily diffusible but which is well adapted for fixation in the cells (glycogen), and gives them up again in a soluble form which is well suited for transportation and for conversion in the tissue cells (grape sugar).

But the subject of carbohydrate, and particularly of glycogen, formation in the body is not yet exhausted.

III. The Formation of Glycogen from Albumin.[3]

It is an established fact that glycogen may be produced from the albuminates, for it has been found that, in animals which have through certain processes (see below) been made glycogen-free, a new formation of glycogen takes place when they are fed exclusively upon albuminoids. Many other facts also, not the least of which are those gleaned in a study of diabetes mellitus in man and of experimental diabetes in animals, bear testimony to the same effect. We are driven, through investigations made up to the present, to the conclusion that a part of the non-nitrogenous atom-groups of the large albumin molecule is always first converted into carbohydrate or carbohydrate-like combinations before it is further burned up into CO_2 and H_2O. In this manner there is formed at least 45 grams of carbohydrate out of every 100 grams of albumin decomposed in the body (Minkowski).

In what part of the body this formation of carbohydrate from albumin takes place is not clear. Many facts point to the liver, many others again speak in favor of the facultative participation of the muscles in this process.

Possibly, as we shall see later, the question of carbohydrate formation (glycogenesis) is not yet exhausted.

IV. Fate of the Carbodydrates in Ordinary Nutrition.

The facts which we have thus far adduced enable us to give a superficial sketch of the final disposition of the carbohydrates.

Under ordinary conditions of nutrition carbohydrate is always at command, the supply being drawn partly from the carbohydrates ingested and partly from the proteids of the food. On the other hand the carbohydrates are always in demand; the cells of the organism, especially the muscle cells, consume them, furnishing by their combustion force and heat. The interposition of reservoirs in the liver and muscles renders possible a finely ordered regulative action, as a result of which the proportion of grape sugar in the nutrient fluid (the blood) remains constant notwithstanding the fluctuating supply. A further very effective arrangement is that the grape sugar, so long as it circulates in physiological amounts in the blood, nowhere passes out with the secretions, more particularly with the renal secretion, except in the merest traces. Were it otherwise, a nutrient material of the greatest value would be wasted.

A deviation from these relations existing under normal conditions of nutrition may occur in one of two directions: 1. The supply of

carbohydrate is insufficient; 2. The supply of carbohydrate is greater than is required.

V. Fate of the Carbohydrates when the Supply is Insufficient (Glycogen Shortage; Sugar Formation from Fat).

When the unequal conditions of a small supply and large demand of carbohydrate continue for a short time only, a few hours or days, the reserve store of glycogen is drawn upon. This, together with what is newly formed from albumin, suffices at first to meet the need of the muscles and sugar-consuming cells, but the supply is finally exhausted if such a drain on the capital continues. Consequently we find only traces of glycogen in the liver and muscle-cells of animals who have been for a considerable time underfed or altogether deprived of food and possibly doing much muscular work at the same time; but if we examine the arterial blood of such animals we find the usual proportion of grape sugar (0.12 to 0.18 per cent.), just as we should if they were fully nourished. The conclusion must be that the organism does not suspend the production of sugar, despite the deficient nutrition; neither is the consumption of sugar interrupted, for whenever any labor is performed sugar is oxidized in the muscles. It is true that a muscle can exercise its functions of work and heat production by means of the consumption of albumin, but a simple calculation will show that the amount of albumin consumed under such circumstances is far from sufficient to cover all the work performed by the muscular system. If we take into calculation all the metabolism and force conversion in the body of men or animals who are doing hard work, in spite of a deficient ingestion of carbohydrates or of a generally insufficient diet, we shall constantly arrive at the same result, viz., that there must be consumed in their muscles a certain quantity of non-nitrogenous substances which can come neither from the reserve supply of glycogen nor from the disintegrated albuminoids, since these two sources together are insufficient to cover the force conversion. The only substance which can meet this deficit is fat. Notwithstanding the great number of investigations directed to this end we do not know at all whether the muscle is able itself to seize upon the fat molecule; but, on the other hand, we do know that during strong muscular action much fat is consumed in the body, a part of this fat being derived from the food and a part coming from the adipose tissue of the organism. We must, therefore, conclude that the fat, before it reaches the muscle, is converted into a form adapted to the purpose which it is to serve. That this form is sugar is shown by the constancy of the blood sugar.

We may also affirm with considerable certainty that the liver is the place where the fat is converted into sugar, when need therefor arises, that is to say, in cases in which neither the carbohydrates nor the albuminates suffice to maintain the proportion of sugar in the outflowing blood at the normal height.

I regard the facultative formation of grape sugar from fat as an absolutely certain fact; I denominate the process "facultative" because it appears to take place only when the supply of carbohydrates is insufficient for the needs of the organism.

VI. Fate of the Carbohydrates when They are Ingested in Excess.

1. *Glycogen Storage.*—The second contingency which we have now to consider is encountered when there is an excessive supply of carbohydrates. When the excess is but moderate and of short duration, there occurs, as we have shown above, a filling of the glycogen reservoirs in the liver and muscles. But the capacity of these reservoirs is limited. It is estimated that about 300 grams of glycogen may be stored up in the human organism. Consequently, if the carbohydrates continue to be ingested in large quantity, and if, at the same time, by reason of a sedentary habit, but a small amount of carbohydrates is consumed in the muscles, the capacity of the storage depots in the body is soon overtaxed. What now happens depends upon circumstances, whether, namely, there is a sudden flooding of the body with carbohydrates, as, for example, when there is single excessive ingestion of sugar, or whether there is a more moderate over-ingestion of carbohydrates continued for a series of days or weeks.

2. *Conversion of Carbohydrates into Fat.*—The last-mentioned case is by far the most frequent. The problem thus presented to the organism is how to dispose of the superfluous material. It solves this problem by converting the excess of carbohydrates, for which there is no more room in the glycogen depots, into fat, and then storing this in the capacious fat reservoirs in the subcutaneous connective tissue and other parts of the body.

3. *Alimentary Glycosuria.*[1]—The process of conversion of carbohydrates into fat requires a certain time, and so it may happen that by repeated accessions so much carbohydrate is taken up into the circulation from the intestinal canal that neither the consumption in the muscles, the storage in the liver and muscles, nor the conversion into fat is sufficient to dispose of the on-pressing stream.

The blood thus naturally becomes abnormally charged with carbohydrates, a condition of hyperglycæmia resulting. We have already

seen that when the percentage of sugar in the blood is normal, neither the kidneys nor any other of the glands excrete more than mere traces of sugar. The condition is otherwise in the case of hyperglycæmia; as soon as the percentage of sugar in the arterial blood exceeds 0.2, the renal filter becomes inadequate and glycosuria results. When I mention about 0.2 per cent. as the limit beyond which glycosuria arises, I do so with a certain reservation. The limit for man is, indeed, not exactly defined and may be subject to certain fluctuations. The fact that the quantitative estimation of sugar in the blood is exceedingly difficult interferes with the more exact determination of this limit. Most of the estimates that we have date from an earlier period when this difficulty was not sufficiently appreciated. The variety of glycosuria which is produced in the manner just described is called *alimentary glycosuria*. It is a purely physiological process and has nothing whatever to do with the disease called diabetes mellitus. It is very important that the physician should have an exact understanding of the mode of origin and significance of alimentary glycosuria, for the diabetic and alimentary forms of glycosuria are often confounded. We may, therefore, briefly set forth here the most important practical points relating to the physiological and alimentary excretion of sugar:

(*a*) Traces of sugar (1 to 2 decigrams to the litre) are, indeed, present in the urine under ordinary conditions of nutrition, but as none of the usual sugar tests gives any indication of this small percentage, healthy urine must be regarded practically as sugar free.

(*b*) Sugar is present in the urine after the ingestion of various saccharine substances, provided they have been taken in considerable amount within a brief period.

(*c*) The sugar appearing in the urine under these circumstances is always of the same kind as that ingested in excess; if it be glucose, for example, we have glycosuria, lactose—lactosuria, levulose—levulosuria, saccharose—saccharosuria.

(*d*) The assimilation limit, that is to say, the limit up to which the in-take of sugar must be raised in order that the urine may become saccharine, varies according to the different kinds of sugar. Sugar appears in the urine after a simple ingestion of:

Milk sugar,	more	than	120	grams
Cane	"	"	"	150–200	"
Fruit	"	"	"	200	"
Grape	"	"	"	200–250	"

The figures given refer to the amounts taken when the individual is fasting; when the stomach contains food the assimilation limit is higher. It is to be understood that these figures are only approxi-

mate, for there are considerable variations in the assimilation limits in different individuals.

(*e*) A positive reaction to the sugar test appears ordinarily in from three-quarters of an hour to an hour after the ingestion of a single large dose, and continues for from one to three hours. The total amount excreted equals, in the case of cane sugar about 2.8 per cent. of the amount taken, of grape sugar 1 per cent., and of milk sugar 0.8 per cent.

(*f*) The assimilation limit for starch is unattainable, that is to say, starch may be taken in any amount without resulting in an excretion of carbohydrates in the urine. Evidently in this case digestion and absorption consume so much time that a sudden flooding of the blood with carbohydrates cannot take place. This is a fact of much importance, for it signifies that those who excrete sugar after the ingestion of starch have a morbidly depressed assimilation limit, and the existence of diabetes mellitus is to be strongly suspected.

4. *Puerperal Lactosuria.*[5]—In the same line with alimentary glycosuria is to be placed puerperal lactosuria. This condition was discovered by Blot in 1850, and later (1877) F. Hofmeister and Kaltenbach showed that the excreted substance was milk sugar. Since that time the term puerperal glycosuria has been abandoned, puerperal lactosuria being employed in its stead. The theory was at once advanced that this lactosuria owed its origin to a process of resorption in the mammary glands, the milk sugar formed in the breasts being taken up with the milk by the blood and excreted unchanged by the kidneys. Further investigations have shown that the affection is encountered when there is an interruption to the withdrawal of milk, as when, because of excoriation of the nipple, a nursing woman has to refuse the breast to the child, or when the infant cannot nurse properly. When, despite an abundant withdrawal of milk, lactosuria is present, the fault lies in a hypersecretion; the affection is observed occasionally in women who secrete such an abundance of milk that they could easily nurse two children instead of one. The sugar generally appears in the urine at the time when a more profuse secretion of milk begins, that is, on the second, third, or fourth day of lactation, and disappears gradually as the child increases the size of its meals.

So far for known facts. That a gland secretion in excess of the needs of the organism may be taken up into the circulation and, in part at least, excreted in the urine, is not without analogy in the organism. I may recall, as an example, the fact that, in an individual who is fasting and, in consequence of insufficient stimulation of the peripheral nerves, secreting but little saliva, a very appreciable

quantity of the salivary ferment (ptyalin) is resorbed and passes out in the urine. The same is true of the waste products of metabolism when, in consequence of obstruction to their outflow, they are thrown back into the circulation (bile pigments and biliary acids). The latter are excrementitious substances and must be removed from the organism under penalty of producing toxic symptoms. In the case of milk sugar the question is different. We have here to do with a substance which is in an eminent degree a physiological nutrient material, a substance which is taken in "milk-cures" to the amount of 100 to 150 grams a day, and which can be ingested by most healthy individuals in single doses of 100 grams and be rapidly absorbed without a trace escaping decomposition and appearing in the urine. Why then should a nursing woman excrete in the urine the certainly very small amount of sugar which she has elaborated in her own mammary glands and which has been thence taken up into the blood? A number of researches which I have made with a view to a solution of this problem have led me to the hypothesis that, in the puerperal state, the capacity of the tissues for breaking up milk sugar is diminished. We have here an instance of adaptation to an end, in that the cells of the mother refuse a material which is pre-eminently suited to the nutritive wants of the nursling.

VII. The Hepatogenous Forms of Glycosuria.

Long before any serious study of transitory alimentary glycosuria in healthy individuals was undertaken, attention was directed to the question whether certain diseases might not depress the assimilation limits for sugar. The following points enter into consideration here:

We know that healthy individuals do not acquire glycosuria after the ingestion of carbohydrates for the reason that the glycogen reservoirs are sufficient to dispose of all the sugar. How is it, then, when these natural carbohydrate storage-places become changed through disease, as in functional and organic disturbances of the liver, of the muscles, or of the nervous system which exercises a controlling influence upon the latter? Are the organs still in condition to fix the glycogen and to prevent a flooding of the blood with carbohydrates?

1. *Experimental Forms* (Following Puncture of the Floor of the Fourth Ventricle, Nerve Injuries, Poisoning, etc.).—In order to reach a just appreciation of the results of clinical investigations, it is necessary to recall the facts which have been brought to light through experimental researches. All these experiments have originated in the celebrated *piqûre* of Claude Bernard. This ingenious investigator demonstrated the fact that a glycosuria of several hours' duration

could be produced in animals by a puncture at the extremity of the calamus scriptorius in the fourth ventricle. After this temporary glycosuria had passed away the liver was found to contain no glycogen.

No glycosuria follows the puncture if the liver has been previously deprived of all or most of its glycogen. This abstraction of glycogen is effected by an enforced fast of considerable duration, chasing the animal about, inducing a pyrexic condition, ligation of the ductus choledochus, or other means.

The interpretation of the experiments, to which there has been scarcely any serious objection, is that from the irritated spot in the central nervous system a centrifugal stimulus is transmitted to the liver, and this stimulus causes the organ to discharge its store of glycogen. It is believed by many that the primary stimulus is transmitted through the vasomotor nerves; others prefer to regard it as a direct action of the nervous irritation upon the hepatic cells. This is a point of secondary importance, however interesting theoretically. *The main fact is the sudden discharge of glycogen from the liver.* The carbohydrate leaves the cells under the form of grape sugar; hyperglycæmia results, and from this arises the glycosuria. We can now understand why the *piqûre* produces no results in animals whose organism is poor in glycogen, and also why the glycosuria, when it occurs, is of short duration, only as long, namely, as the supply, whether abundant or scanty, of glycogen contained in the liver holds out, and until the excess of sugar thrown out into the blood is eliminated or consumed.

After Claude Bernard's experiments investigation was zealously turned in this direction, and in the course of time many other influences have been discovered which are effective in the production of temporary glycosuria. Among these the following may be mentioned: destruction of the superior and inferior sympathetic ganglia in the neck, of the first thoracic ganglion, of the abdominal ganglia, and of other sympathetic nerves; painful stimulation of the peripheral nerves; psychic disturbances; lesions of various portions of the cerebrum, mid-brain, and cerebellum. It seems to be possible, indeed, to produce glycosuria by a sudden, strong, paralyzing or exciting injury of any part of the nervous system. Nevertheless no absolute dependence can be placed upon the results of experiments either in man or in animals. Glycosuria is obtained in certain experiments on animals and is observed after certain acute traumata in man (for example, after apoplexy), while in other cases, in conditions apparently exactly similar, this result does not follow. A stimulus applied to the place designated by Claude Bernard is alone to be absolutely relied upon to produce the expected result.

Next after these gross mechanical lesions of the nerves are certain poisons to be named as productive of glycosuria; these are carbonic oxide, carbon disulphide, curare, morphine, strychnine, nitrobenzol, nitrite of amyl, and others. Asphyxiation, profuse hemorrhage, and intravenous injections of dilute salt solutions are frequently productive of the same result.

Whenever under such and similar conditions glycosuria is produced, an abundant supply of glycogen must be presumed to be present in the liver; in badly nourished, glycogen-poor individuals this result is not observed. In any case the duration of the glycosuria is measured by hours only.

There can hardly be any doubt that all the above-named injuries, and others similar to them, act in the main in the same way as the puncture at the floor of the fourth ventricle, viz., they lead to a discharge from its reservoir of the previously formed glycogen, either by a direct influence upon the liver itself or indirectly through the intervention of the nervous system. Since the liver enters especially into consideration here, I have called all these forms of glycosuria "hepatogenous."

2. *Clinical Forms* (Alimentary Glycosuria complicating other Diseases).[6]—Possibly some of these experiments may have a bearing also upon true diabetes mellitus in man, but that is a point that cannot be considered here. We have primarily to determine how far these facts throw light upon glycosuria occurring in the course of other diseases, a condition to be clearly differentiated from true diabetes. The facts teach us that, under certain conditions, the glycogen reservoirs become, as it were, too narrow to hold large amounts of this substance. Does this storage insufficiency play any clinical rôle? In studying this question the attention of clinicians will be directed especially to diseases of the nerves, muscles, and liver, disturbances of the circulation (passive congestion of the liver), and poisoning. Indeed, we are already in possession of a series of facts in human pathology which are so closely related to the results of animal experimentation that we can scarcely doubt that we have to do with identical processes.

In this category belong the rare transitory glycosurias following concussion of the brain (A. Fischer), cerebral apoplexy (Ollivier, von Frerichs, Schütz, Loeb, and others, and three personal observations of the author), severe neuralgia, and disturbance of the mental balance. In these cases the glycosuria lasts usually a few hours only, or at most a few days. It is nevertheless in just these cases that it is difficult to draw the line between transitory glycosuria and diabetes mellitus, for, in the first place, many of these acute neurogenous forms of glycosuria pass over into chronic diabetes (Frerichs),

and secondly, many instances are on record in which individuals had suffered from temporary glycosuria following the influences above mentioned, and then subsequently, sometimes years later, acquired unmistakable diabetes mellitus. In these individuals apparently a latent diabetic disposition slumbered for a long time, to be awakened—at first only temporarily—by nervous influences. The whole history of acute neurogenous glycosuria and daily repeated experiences teach us that individuals react in very varying degree to the above-mentioned influences. The individual predisposition appears to be of more importance than the special form of lesion inflicted.

In this group belong also the acute forms of glycosuria, almost always disappearing in a few hours, which follow poisoning by certain substances, such as morphine, hydrocyanic acid, mineral acids (rarely), nitrite of amyl, carbonic oxide, chloralamid, nitrobenzol, anilin, ergotin (one case observed by the writer), etc. Here also are to be mentioned the rare instances of acute glycosuria described by Gans and Finkler as occurring during an attack of biliary colic. This form finds its analogy in the experiment of ligating the bile duct, which is followed by a rapid discharge of glycogen from the liver.

In view of the rare occurrences of spontaneous glycosuria in organic disease, the attempt has often been made to gather data relating to the sufficiency or insufficiency of the glycogen depot in various affections, by the exhibition of large amounts of sugar. As a rule grape sugar has been selected, in doses of from 150 to 200 grams—not more, since with larger doses even in healthy individuals a transitory glycosuria is produced (see page 43).

The results of these numerous clinical experiments are not concordant. If we take into consideration, however, those investigations only in which proper methods for the estimation of sugar have been employed, we are brought to the conclusion that glycosuria can be induced in all these diseases with scarcely greater facility than in healthy individuals, or, in other words, an insufficiency of the glycogen reservoir can hardly be said to exist.

To come to special diseases: Affections of the brain, spinal cord, peripheral nerves or muscles, and functional nerve troubles do not favor the production of alimentary glycosuria; Basedow's disease alone does so. Diseases of the liver: In certain cases of cirrhosis glycosuria was easily produced, but in the great majority of these cases, as also in all other forms of hepatic disorder, it was not. This is the more remarkable as in most of these diseases the hepatic tissues adapted to the taking up of glycogen were deeply affected. In order to reconcile the apparent contradiction between the results of

experiments on animals and clinical experience, we must remember that the liver is not the only organ which stores up glycogen, but that the muscle-cells and glands likewise possess this property. Possibly these bodies act vicariously for the liver in case of necessity. The question is theoretically plausible, but up to the present it has not been seriously handled. In diseases of the lungs and heart and in the secondary affections resulting therefrom (hyperæmia of the liver, atrophic conditions, fatty liver), and also in diseases of the blood, positive results are even more rare than in primary hepatic disorders.

The study of alimentary glycosuria in diseases of the glycogen-storing organs may be regarded now as fairly completed, and a multiplication of investigations into this question is hardly needed. It was expected that they would lead to a better understanding of diabetes, but this expectation has proved unfounded. The most important fact which we have been able to gather from them is that the due consumption of carbohydrates in the body is not dependent upon the integrity of the liver, for the most serious diseases of this organ cause no spontaneous, and but seldom an insignificant alimentary, glycosuria. From this we can understand why it is that theoretical writers on the subject of diabetes, who formerly referred to the liver with the greatest reverence, have come more and more to disregard this organ as a disease centre.

VIII. Glycosuria in Phloridzin Poisoning.[7]

The form of glycosuria which we are about to study, namely, that occurring in phloridzin poisoning, has thrown no greater light upon the problem of diabetes than did the experiments which we have just considered. Yet our acquaintance with it has added in an important degree to our knowledge of the process of sugar formation in the animal organism. Phloridzin is a glucoside obtained from the bark of the root of apple and cherry trees. In 1886 v. Mering announced that after the administration of this substance to dogs and rabbits there was an excretion of a large percentage of sugar in the urine. A few hours after the exhibition to dogs of about one gram of phloridzin to every kilogram of the animal's weight, the urine is found to contain 10 per cent. or more of grape sugar. The glycosuria persists as long as the administration of phloridzin is continued. The same result can be obtained also in the human subject, in whom the ingestion of phloridzin produces no injurious consequences. The sugar appears in the urine indifferently whether carbohydrates have been previously ingested or whether the individual be fasting or

living upon a flesh diet. In experiments upon animals sugar was excreted even when the dogs had been fasting so long that no glycogen, or at most only traces, could have been present in the liver or muscles. We see here, therefore, a very remarkable difference between the previously described forms of glycosuria and that which follows phloridzin poisoning, and recognize at once that the occurrence of the two forms must be very differently explained. More exact investigations have furnished this desired explanation. Other observers as well as v. Mering found that the blood was poor in grape sugar during the phloridzin glycosuria, a condition of this fluid exactly the opposite of that which exists after *piqûre* and overfeeding. There is now scarcely any doubt that phloridzin acts primarily upon the kidneys, so changing the renal epithelium as to destroy its normal power of keeping back sugar and to cause it to seize greedily upon the sugar held in solution in the blood. Hence comes it that the blood is found to be poor in sugar. This drawing of sugar from the blood is at once met by a discharge from the glycogen reservoirs, and when the supply of glycogen is exhausted new sugar is formed in order to maintain the percentage of sugar in the blood, which is a matter of so great importance, at its normal height. Under these conditions albumin is used for the sugar production, either the albumin of the food or, when the individual is fasting, the albumin of the tissues.

The study of phloridzin diabetes has, more than all other previous researches, established the certainty that the albuminates may become a source of sugar production. It has not yet been definitely settled whether or not fat also may be drawn upon as an adjuvant in furnishing a supply of sugar to the blood, in case of phloridzin poisoning.

The lesson of phloridzin poisoning is important from another point of view. It has pointed out to us an entirely new way, and one that is full of surprising aspects, by which glycosuria may be produced. We have as yet, however, no ground for the assumption that the clinical affection, diabetes mellitus, ever arises in this way. Still we must remember that, in the history of diabetes mellitus, the view has often been expressed by well-known authorities that this is a primary affection of the kidneys. For example, Dickinson treats of diabetes mellitus in his work on "Diseases of the Kidneys," published in 1875, and in earlier times we meet with this opinion still more frequently (Galen, Theophrastus, Paracelsus). The present has offered a long-deferred reparation to these authors in so far as it has been shown by phloridzin poisoning that there is a form of glycosuria and even, if one cares to use the term, diabetes mellitus,

which is dependent upon disease of the kidneys. This experience warns us not to reject absolutely the possibility that such a pathogenesis may be present in true diabetes mellitus. As was said above, we have not the slightest ground for such an opinion; but it is possible that there are other poisons, gaining access to the human organism in some manner unknown to us, which may produce changes in the kidneys similar to those caused by phloridzin. The doctrine, which has indeed for a long time been questioned, that diabetes mellitus is a morbid entity, can now no longer be upheld on theoretical grounds.

IX. Experimental Pancreatic Diabetes.[8]

Of much more far-reaching significance, and of immense importance for the fundamental doctrines of biology, is another form of experimental glycosuria. This is the diabetes mellitus occurring after extirpation of the pancreas.

I employ here for the first time the term "diabetes mellitus" to designate an artificially produced glycosuria. I have hitherto intentionally avoided the expression because we have until now been considering a rapidly evanescent excretion of sugar which survived hardly more than a few hours the injuriously acting interference. In the case of extirpation of the pancreas, however, things are different; for we have here as the result a chronic disease which continues to the end of life.

After many clinical facts bearing upon the relation between pancreatic disease and diabetes mellitus had been recorded (Lancereaux and others), and after many experimenters had endeavored with little or no success to cause a glycosuria by extirpation of the pancreas, division of the nerves supplying the organ, or ligation of the pancreatic duct, the question was taken up anew and elucidated by v. Mering and Minkowski (1890). We are ready to give full credit to the Italian scientist de Dominicis for having undertaken, simultaneously and independently of the above-named authors, the same researches and for having arrived at practically the same results. Nevertheless, from a biological standpoint he did not treat the question so well or so carefully as did v. Mering and Minkowski, and consequently his investigations had less influence upon the further development of this important question.

When the pancreas of a dog is completely extirpated a severe form of diabetes is developed within twenty-four hours, which leads to the death of the animal in a few weeks. The disease is denominated "severe" because the excretion of sugar continues even when all carbohydrates have been abstracted from the food. The disease thus

produced resembles in every particular grave diabetes in man, for, besides the chronic glycosuria, we find polyphagia, polydipsia, polyuria, hyperglycæmia, excessive destruction of albumin, emaciation, loss of strength, excretion of large quantities of aceton, acetoacetic acid, oxybutyric acid and ammonia, coma and death. The sugar excreted is, as in the disease in man, grape sugar.

Besides the discoverers of the affection, the following investigators have made contributions to our knowledge of pancreatic diabetes: Lépine, Arthaud, Butte, Remond, Hédon, Gley, Thiroloix, and Lancereaux in France; de Dominicis, de Renzi, Reale, and Gaglio in Italy; and Aldehoff and Sandmeyer in Germany. Some of these authors have been unable to confirm in every respect the accounts of the discoverers, since they were not always fortunate enough to induce diabetes or were able to cause a transitory glycosuria only. Minkowski, however, has shown conclusively that all these failures to produce the expected result were to be explained by defective methods of research. Extirpation of the pancreas in the dog is, indeed, an uncommonly difficult operation; small portions of the gland may very readily be left in the body, and are with difficulty to be discovered in the cicatricial tissue at the subsequent autopsy. But when the pancreas has not been entirely removed the occurrence of diabetes is not to be expected (see below).

Omitting minor details, the most important points which have been established concerning experimental pancreatic diabetes are the following:

1. Diabetes has, up to the present, been artificially produced by extirpation of the pancreas in the following-named animals: dogs, cats, pigs, carnivorous birds, frogs, and turtles. Most of the experiments, however, have been carried out upon dogs, and what follows relates to the results of experiments upon this animal.

2. Diabetes occurs in dogs only when the pancreas has been totally removed, but then regularly. Assertions opposed to this statement are growing constantly fewer, while those in agreement therewith are as steadily increasing in number. The same results have been commonly, though not invariably, obtained after the injection of warmed paraffin into the duct of Wirsung. The paraffin hardens upon cooling and plugs up the ducts, the result usually being complete atrophy of the entire gland.

3. When the pancreas is partially extirpated and the remaining portion, with its vessels attached, sutured to the abdominal wall (*greffe sous-cutanée*), diabetes fails to appear; but if this engrafted portion of the pancreas is removed later by a now insignificant operation, the disease manifests itself. This modification of the experi-

ment proves that accidental injuries of the sympathetic nerves, etc., which are often unavoidable in intra-abdominal total extirpation of the pancreas, have nothing to do with the production of the diabetes; and more than that, it proves that it is only the removal of the pancreas itself that is responsible for the disease.

4. When about a tenth part of the pancreas is left in a functionating condition, a mild form of diabetes ensues. The glycosuria is slight and occurs only after the ingestion of carbohydrates. But if the remaining portion of the gland becomes subsequently obliterated, then diabetes in severe form follows. When more than one-tenth of the gland is left behind with power of performing its functions, no diabetes ordinarily results.

5. The relation which exists between the pancreas and excretion of sugar from the organism does not depend upon the action of the pancreatic juice, for diabetes does not occur in cases of simple shutting off of the latter from the intestine, nor yet when the fluid escapes through a cutaneous fistula.

6. The influence of the pancreas upon the excretion of sugar appears to be, at least in dogs, a specific one, that is to say, no organ other than the pancreas possesses it. Some authors (de Renzi and Reale) have, indeed, asserted that they obtained the same result through extirpation of the salivary glands and through resection of the entire duodenum. Nevertheless Minkowski, in corroboration of earlier experiments of Fehr, failed to observe this. It is true that sometimes, even in his hands, glycosuria appeared after the operations just mentioned; but it was only moderate in degree and rapidly disappeared, acting exactly like those forms of glycosuria observed after numerous operative procedures in animals (see above); it was an experimentally produced glycosuria, but not diabetes mellitus.

We see, now, from the above-enumerated experimental facts that, in the body of the dog (and probably also of many other animals), the pancreas is necessary for the regulation of the normal sugar economy. After excluding all other possibilities, the discoverers have formulated the following hypotheses:

Either some substance, which has an injurious influence upon the conversion of sugar, collects in the organism after extirpation of the pancreas, or else, after this operation, there is some substance wanting or some function is abolished which under normal conditions serves to facilitate the conversion of carbohydrate bodies.

The expressions in these formulas are very general and indefinite, but that is of necessity, since great caution is demanded in pronouncing upon these questions. Something definite can nevertheless be said as to the way in which the economy of the carbohydrates is dis-

turbed by extirpation of the pancreas. In all the experiments made the fact is evident that the grape sugar taken in with the food, as well as that found in the organism itself, is no longer consumed in a normal way after removal of the pancreas, while there is no evidence going to show that there is also a morbidly increased new formation of sugar. The important point is therefore established that the deposit of glycogen in the liver and muscles does not normally take place after extirpation of the pancreas. The animals may be fed abundantly with starchy materials without more than traces of glycogen being found in these organs. The only exception to this is when the animals are supplied with levulose (fruit sugar); in this case the liver and muscles become richly supplied with glycogen. This last-mentioned fact is especially interesting since clinical experience has long since shown that the human subject of diabetes mellitus suffers from only a slight increase of sugar in the urine after the ingestion of levulose (see below). The assumption that there is a certain internal relation between a diminished deposition of glycogen and a diminished consumption of carbohydrates in the organism receives some support from this experience.

Naturally the endeavor has been made to obtain a more profound theoretical understanding of the way in which these results of extirpation of the pancreas are brought about. But up to the present Lépine of Lyons is the only one who has pursued the subject further along experimental lines. His theory is that the pancreas produces a ferment which enters the circulation and causes a breaking up of the grape-sugar molecule within the blood. Lépine calls this substance "glycolytic ferment." After extirpation of the pancreas this ferment is not present; the sugar therefore accumulates undestroyed in the blood and from the hyperglycæmia so produced glycosuria results. The experiments upon which Lépine bases this opinion, which were carried out for the most part in collaboration with Barral, were conducted in the following way. He abstracted a certain amount of blood from the vascular system, and immediately heated the half of it to 54° C. (129.2° F.), destroying thereby the glycolytic ferment. He then put this portion of the blood, as well as the remaining portion which had not been heated, into an incubator in a temperature of 39° C. (102.2° F.), and examined both samples for sugar after the lapse of an hour. When Lépine used the blood of healthy animals and men, he found a much smaller percentage of sugar in the not-heated than in the heated sample of blood; but when the blood of an animal from which the pancreas had been removed was taken, the difference in the proportion of sugar contained in two samples was slight. He reasoned from this that there was a decrease

in the amount of glycolytic ferment after extirpation of the pancreas. He also extended his investigations to men, and found that the conditions were the same in individuals suffering from diabetes mellitus as in dogs without the pancreas.

If Lépine's researches had been rightly made, and if we could accept the conclusions which he derived from them, they would constitute a most important advance in our knowledge of pancreatic diabetes. But the matter is not so favorable. In the first place it must be remarked that many well-known investigators, skilled in chemical manipulations, have repeated Lépine's experiments without obtaining his results. Among these are Arthus, Gaglio, Seegen, Kraus, and Minkowski. The contradictions relate to the fact alleged by Lépine of the rapid disintegration of sugar in normal blood, as well as to the assumed difference in this respect between normal and diabetic blood. It has further been held that we cannot argue from the results of test-tube experiments as to the conditions present in living blood circulating in the vessels of the body. Without doubt the whole question demands further study and elucidation, but it cannot be denied that at present the weight of opinion is opposed to Lépine's theory.

From the description just given of the experimentally produced pancreatic diabetes it can well be seen that the discovery of von Mering and Minkowski is of very great importance. It will be our task later to determine how much light has been thrown upon the question of the etiology of diabetes mellitus in man by the results of these experiments.

THEORIES OF DIABETES MELLITUS.[9]

In the previous sections, especially in the discussion on experimental pancreatic diabetes, I have with few exceptions used the expression that glycosuria depends upon a disturbance of the carbohydrate economy; but on the other hand I have purposely spoken as little as possible of the way in which the economy is disturbed. It is evident that a disturbance of equilibrium may be brought about through:

1. Over-production of sugar;
2. Under-consumption of sugar in the body; or
3. The two processes acting in concert.

For a number of decades there has been a conflict of opinion as to which of these deviations from the norm, or whether both together, play a causative rôle in diabetes. We are now in position to affirm very positively what happens in certain forms, at least, of glycosuria.

I. Theory of an Over-Production of Sugar.

Taking the term "over-production" in a rather comprehensive sense, it is unquestionable that it enters into consideration in all acute forms of glycosuria following upon an over-ingestion of carbohydrates. This follows immediately from the description of alimentary glycosuria and its origin which I have given above.

We can also speak of "over-production" in those forms of glycosuria occurring in man and animals which result from the irritations and injuries of the nervous system, of which *piqûre* is the type; also probably in those forms occasioned by any of the intoxications of which carbonic oxide poisoning is the type. But in all these cases we have to do merely with an over-production of grape sugar from already existing glycogen, apparently never, however, with an abnormally increased new formation of carbohydrates from other substances. We had, indeed, seen in what close relation all these forms of glycosuria stand to a repletion of the glycogen reservoirs, and how constantly they fail to be produced when there is no previously formed store of glycogen to draw upon.

We have undoubtedly to do with "under-consumption" and "over-production" in phloridzin diabetes. In this case the sugar is not consumed but is drained away from the blood through the kidneys. In order to compensate for this loss of nutritive material by the blood, there follows an increased production from the glycogen at hand, and, when this supply is exhausted, from the albuminates.* The under-consumption is therefore the primary condition, over-production being secondary. We must leave it a mooted question whether similar conditions ever play a part in human pathology.

There remains for consideration pancreatic diabetes and diabetes mellitus in the human subject. The question here is a more complicated one and we must arrive at its solution in a roundabout way. And first we must get a clear conception of normal sugar production.

The blood draws its sugar:

1. Certainly from the carbohydrates of the food.

2. Certainly from the albumin split up in the body, in the proportion of at least 45 grams of sugar to every 100 grams of albumin. In 100 grams of albumin there are 16 grams of nitrogen, and as all the nitrogen of the decomposed albumin appears in the urine, so we have 45 grams of newly formed sugar for every 16

* I regard it as probable, also, although this view is contrary to that held by all other writers, that a very considerable quantity of sugar is formed from fat in cases of extreme phloridzin poisoning.

grams of nitrogen excreted in the urine—or 2.8 grams of sugar for each gram of nitrogen.

3. Possibly for every gram of nitrogen in the urine (representing 6.25 grams of albumin) more than 2.8 grams of sugar are formed.

4. Possibly also sugar is normally formed from fat (see page 41).

We have, therefore, two certain and two hypothetical sources of sugar production in the body. Let us consider only the first two. It is evident that *an abnormal, that is, increased, production of sugar is to be assumed as most certain when the glycosuria answers to the following formula:*

Sugar in the urine > sugar of the food + (nitrogen in the urine × 2.8).

As a matter of fact the quantity of sugar in the urine in pancreatic diabetes never rises above the value expressed by the second half of this formula (Minkowski). The same is true in still greater degree in diabetes in man when the diet is poor in carbohydrates—even in the severest forms of the disease. When, however, an individual with profuse glycosuria ingests a large amount of carbohydrates the quantity of sugar excreted may temporarily reach the height given in the formula, but that occurs only on single days and never continues for long periods. And as only cases of long duration could serve as a basis upon which to found conclusions, we are unable to gather anything from the metabolism of the diabetic in support of the theory of over-production.

II. Theory of an Under-Consumption of Sugar.

I forego a criticism here of the other arguments advanced in support of the theory of over-production, for they are all of them vulnerable; they are, if I may be allowed the expression, "sentimental arguments" (*Gefühlsgründe*). We will therefore turn our attention to the theory that the carbohydrates introduced or newly formed in the body of the diabetic fail to find their normal application. This is again a very general and indefinite expression. I employ it intentionally because in truth the theory can hardly be further extended without leaving the secure ground of facts. Nevertheless it is permissible to call attention to the fact that the normal employment of sugar in the economy may be interfered with in a number of different ways.

1. *Insufficient Capacity of the Glycogen Reservoirs.*—We may conceive that in diabetes the physiological glycogen magazines are not at all, or only to a limited degree, capable of furnishing a place for the storage of the carbohydrates which have gained access to the circulation, and that consequently the sugar, as much of it as is not used by

the working cells of the body (glands, muscles, leucocytes, etc.), is seized upon by the kidneys and excreted. We may conceive that the morbid state of the glycogen depots may be caused by nervous irritation, the presence of toxic substances, or the absence of certain ferments (the ferment of the internal secretion of the pancreas?).

This theory is, in its fundamental parts, very old, but it has fallen into discredit since it has come to be shown how seldom severe parenchymatous diseases of the liver are associated with spontaneous or alimentary glycosuria. It must, it is true, be remembered that in the case of hepatic disease there are still glycogen reservoirs remaining in other glands and in the muscles, and that the capacity of these may upon occasion be enlarged to compensate for loss of storage room in the liver. The theory must, therefore, not take into consideration the liver only, but must assume that besides this organ the other glycogen depots also have become insufficient.

If all the glycogen reservoirs become insufficient there must indeed result, even under normal conditions of sugar production, a hyperglycæmic state and glycosuria corresponding closely to what is seen in diabetics. The deficient appropriation of sugar would be the result of its unequal distribution in the body and of a disturbance of the regulating apparatus.

2. *Insufficient Consumption of Sugar in the Tissues.*—It may be conceived that, while the normal functions of the glycogen reservoirs remain intact, the cells of the body may have lost in whole or part their capacity of seizing upon the sugar molecule. In such a case the sugar passes in a normal way from the intestinal canal into the blood, and may also be deposited normally in the liver, muscles, etc., but its further appropriation is interfered with. It is carried past the cells without being taken up by them at all, or at most only partially, collects in the blood, the amount being constantly increased by new accessions from the carbohydrates of the food and by the sugar newly formed from albumin, and is then excreted through the kidneys. It remains as yet undetermined what the nature of the injury is through the action of which the cells and tissues suffer in their sugar-consuming power. It may be due to nervous influences, or again it may be the result of an absence of a ferment (perhaps furnished by the pancreas), or of a mixture of some poisonous substance with the blood.

This theory of a diminution of the sugar-consuming power of the tissues has received very strong support in the results of investigations into the gas interchange during respiration obtained by Leo and Hanriot as well as by Weintraud and Laves. It is known that the individual subsisting on a mixed diet gives out less carbonic acid gas

(CO_2) than he receives oxygen (O_2), the ratio being on an average 9:10. This is expressed by the fraction 0.9, and is called the "respiratory quotient." This quotient becomes greater when increased amounts of carbohydrates are consumed in the body, as for example after a meal rich in sweets; it becomes smaller, approaching 0.7, when a larger amount proportionately of albuminates and fats is consumed, as for example after the ingestion of these substances or after a long fast. Now the above-mentioned authors found that in diabetics, who were fasting, the respiratory quotient was considerably depressed, and that, contrary to what is observed in healthy subjects, it was not appreciably increased by the ingestion of carbohydrates. This observation has a wide bearing, and can hardly, without doing violence to the facts, have any other significance than that the cells of the diabetic organism refuse to perform their sugar-consuming function.

These results are, it is true, in direct contradiction to those obtained by the experiments of Chauveau and Kaufmann. The latter examined the blood of the crural artery and veins in healthy and diabetic dogs to determine the percentage of sugar. The difference in the amount of sugar between the arterial and venous blood was the same in both healthy and diseased animals, and they therefore concluded that the capacity of the tissues for consuming sugar is not lost in diabetes. There is much to be said, however, against the significance of these experiments; and especially may it be urged that the sources of error in the sugar analysis of the blood are so great, even when this is undertaken by skilful chemists, that conclusive results could not possibly be obtained by the method of Chauveau and Kaufmann.

An objection against this theory may also be found in the way in which glycogen acts in the diabetic organism. If we had to do only with a lowered sugar-consuming power, then the glycogen-storage reservoirs would necessarily always be taxed to their fullest capacity. Their overfilling and resultant overflowing on the one hand, and the slight consumption on the other, would be the cause of the hyperglycæmia and glycosuria. But as a matter of fact the organs of both men and dogs suffering from diabetes invariably contain but little glycogen (Frerichs, von Mering and Minkowski).

Another objection to this as an all-embracing theory is, that if a diminished consumption of sugar in the cells were the exclusively active factor in the production of diabetes there would still be another application to which the sugar could be put, viz., conversion into fat. But this way is also evidently wholly or in great part closed when diabetes exists (see the section on the relations between diabetes and obesity, p. 66).

III. Theory of a Combined Action of the Two Disturbances.

When we consider the difficulty of explaining diabetes mellitus by an insufficiency of the glycogen reservoirs or by an insufficiency of sugar consumption alone, we must assume that both these factors act in concert. Possibly now one factor, now the other, preponderates, according to the etiology of the individual case.

If from this standpoint we look back upon the outcome of our observations, the answer to the question, what is to be understood by a "diminished consumption of carbohydrates," would be:

The diminished consumption arises from an interworking of the following factors:

1. Inadequate distributions of the carbohydrates in the body (insufficiency of the glycogen reservoirs);

2. Diminution of the property residing in the tissues of seizing upon and breaking up the sugar molecule;

3. Diminution of the property residing in the tissues (certain special tissues) of compressing the sugar molecule into a fat molecule.

For my part I am of the opinion that we can dispense with neither of these three points in the explanation of the details of the process. As, however, it is altogether impossible to reach a just appreciation of the bearing of each of the three factors above enumerated upon individual cases of the disease, I prefer in future to employ the general term "diminished employment or consumption of the carbohydrates," and to leave it to the reader to decide for himself whether the one or the other is the essential factor.

IV. Review of the Theories of Glycosuria.

We may summarize the conclusions deduced from the discussion upon which we have been engaged in this section as follows:

1. There are forms of glycosuria which are due to "over-production," using the term in its broader sense; these are

a. Alimentary glycosuria. This form has nothing to do with the disease, diabetes mellitus.

b. Acute glycosuria following injuries to the nervous structures and poisoning by certain substances (sudden emptying of the glycogen reservoirs).

2. There are forms of toxic glycosuria in which under-consumption is joined to over-production (phloridzin diabetes). Both these disturbances are in this case the result and not the cause of the glycosuria. Whether similar cases occur in human pathology is uncertain, although very possible.

3. Glycosuria resulting from an over-production of sugar from albumin and fat is not known to exist. Over-production plays no part in diabetes mellitus in man.

4. Glycosuria due to diminished consumption of carbohydrates is an established fact. It is immaterial what may be regarded as the causative factor of this diminished consumption, it stands in the foreground in experimental pancreatic diabetes, and probably also in the great majority of cases of diabetes mellitus in man.

ETIOLOGY OF DIABETES MELLITUS.

I. Geographical Distribution; Conditions of Nutrition.

Diabetes mellitus is found in every country, but apparently it does not prevail to the same extent in all. It is difficult to obtain reliable figures, for the statistical material of different countries bearing upon this point has not yet been sufficiently worked up, and we have to gather our information from the personal experience of individual writers rather than from national tables of morbidity. Southern Italy and India are regions in which diabetes mellitus appears to be especially frequent. Many writers refer the prevalence of the disease in these countries to the preponderance of vegetable food, and particularly of saccharine fruits, in the diet of the inhabitants; but it is very questionable whether such a view of the relation of cause and effect is justifiable, for the use of vegetables as the main food of the people is widespread throughout the globe, and is the rule in many regions in which diabetes appears not to prevail to any unusual extent. On the other hand, Sweden is counted among the lands in which diabetes is very common, although its inhabitants do not indulge in carbohydrates to any excessive degree. Furthermore it may be said that in Germany at least, and apparently in other countries also, the well-to-do members of the community suffer from diabetes in far larger proportion than the poorer classes. When we consider the difference in the food of the two classes, we must admit that this fact argues very strongly against the theory that there is any definite relation between the occurrence of diabetes and an excessive consumption of carbohydrates.

II. Race.

Something a little more definite may be said concerning the preference of diabetes for certain races. The Semitic race is in an especial manner predisposed to this disease. Whether this is true of all the branches of the Semitic race must remain uncertain, but the fact

may be asserted with positiveness concerning the Hebrews scattered throughout Europe. The causes for this special predisposition of the Jews are as obscure as are other racial peculiarities, and we can offer only conjectures.

III. Sex.

There is a marked difference in sexual predisposition, all the facts pointing to a special liability of males to suffer from diabetes. From the statistical material at hand I may quote the figures of Frerichs and Seegen. The former, among 400 patients with diabetes, found 118 women; the latter, 232 women out of a total of 938 patients. Similar figures have been published by other observers.

IV. Age.

Age is also of decided etiological significance. Diabetes occurs, indeed, at any age; even nursing infants have been observed to suffer from the disease, but such cases are very rare. The affection becomes a little less infrequent about the age of puberty, yet even here it is of uncommon occurrence. The disease when it occurs in children is very often the result of hereditary influences; one frequently sees several children of the same family affected. Diabetes in children is also worthy of note from a prognostic point of view, for it occurs for the most part in severe form at this age and runs a rapid and inevitably fatal course. There are, however, exceptions to this rule, as R. Schmitz[10] has recently shown in his noteworthy monograph.

After puberty is passed diabetes increases rapidly in the frequency of its occurrence, although the highest figure is not reached until the fifth decade of life. The facts, however, upon which this statement rests are not altogether reliable. The ages given by different observers are those of the patients when first coming under observation, and there are no figures to show when the disease began; but the beginning of the affection may often date back many years.

Toward the end of the sixth decade of life diabetes becomes again of less frequent occurrence, not only, it would seem, absolutely but also relatively to the number of individuals living at this age. When the disease makes its appearance in men at the prime of life or on the threshold of old age, it is usually in very short persons whose obesity has existed for ten or twenty years and now becomes complicated with diabetes. The disease is seldom very severe when it is developed at this age. In woman there is an increase in the frequency of diabetes at the climacteric period (Bouchardat).

The following table shows the frequency of the disease at different ages, according to the experiences of Frerichs and Seegen:

	Percentage of Frerichs' cases.	Percentage of Seegen's cases.
Under 10 years.....	1.	0.5
From 10–20 "	7.	3.
" 20–30 "	10.	16.
" 30–40 "	18.	16.
" 40–50 "	25.	24.
" 50–60 "	26.	30.
" 60–70 "	11.	10.
Over 70 "	1.	0.5

V. Heredity.

Hereditary influences are of significance in the etiology of diabetes, although by no means to such a degree as in obesity and gout. The direction in which heredity acts is variously estimated by different writers, unanimity existing only in relation to a few points. Among these are the already mentioned prevalence of the disease among Hebrews and the comparatively frequent seizure of children of the same family at an early age or even in infancy. On the other hand individuals whose parents are or were sufferers from diabetes are attacked comparatively more rarely. The influence of heredity is much more apparent when we take into account the morbid history not only of the direct ancestors but also of the other relatives (uncles, aunts, and cousins). Tracing the history in this way Frerichs was able to assert the influence of heredity in 10 per cent. of his cases, Seegen in 14 per cent., Schmitz in 20 per cent., and Bouchard in 25 per cent.

Many authors search still further after an hereditary taint, outside of the actual occurrence of diabetes, and note the frequency of other constitutional affections in the families of those suffering from the disease. A family history of obesity or gout is regarded as of especial significance. Cases are reported in which the grandfather was diabetic, the son gouty, and the grandson again diabetic. That may be called hereditary alternating diabetes.

VI. Contagion.

There are some remarkable cases reported in the literature of this disease which speak in favor of the possible transmission of diabetes from one individual to another. To the late R. Schmitz is due the credit of having directed attention to this possibility. Out of his rich experience (2,320 cases of diabetes) he was able to gather 26 in-

stances of this kind. Persons known to be in perfect health, with few exceptions married people and usually the wives, became diabetic after having for a long period taken care of a person with diabetes, living with him continuously in intimate relations, sleeping in the same room, and often kissing him. In not a single case could hereditary influences be alleged, and in no instances was the one last attacked related by blood to the first sufferer. Furthermore there was nothing else that could be looked upon as a cause for the occurrence of the diabetes; the persons had never indulged especially in sugar, they had not suffered from gout, nor was it possible to allege any other etiological moment. Schmitz opens the question, therefore, whether there is not a special form of diabetes which can be transmitted from one person to another. Similar instances are related in the monographs of Reil and Th. Henke, Bouchardat, Seegen, and in numerous reports of single cases of diabetes. Generally speaking, however, this mode of origin of the disease, if ever active, is extremely rare. And, furthermore, the possibility of the transmission of diabetes from one individual to another is strenuously contested (Senator), the instances alleged by Schmitz being explained by the fact that persons living together are naturally exposed to the same injurious influences.

VII. Occupation.

The fact that the disease occurs with unequal frequency among the well-to-do and cultured classes on the one hand and the poorer and laboring classes on the other points to the decided etiological influence of occupation. It is generally acknowledged that diabetes attacks city dwellers with greater frequency. Still it must be remembered that the disease when attacking those who live in cities is generally much earlier and more certainly recognized, while in the country many cases of diabetes occur which are never diagnosed, and only too often pulmonary consumption appearing later is looked upon as the primary disease.

More certain is our knowledge of the distribution of diabetes among the different classes of those living in cities. In Berlin the absolute number of cases in the upper ten thousand is greater than that in the lower hundred thousand, and the same proportion is said to exist in London. In other words, wealth and culture increase the liability to diabetes tenfold.

Among occupations, those predispose especially to the disease which involve exhausting intellectual labor and mental excitement. Among diabetic sufferers we find a striking number of scientists, musicians, poets, teachers, statesmen, merchants, and speculators.

And then again the disease attacks with special predilection those who lead a luxurious, aimless, idle, and unintellectual existence. *Les extrêmes se touchent!*

VIII. Psychic Influences.

We have just spoken of the effect of psychic influences in as far as intellectual activity is related to occupation, yet much remains to be said of the bearing of the mental condition upon this disease. It may be remarked at the outset that individuals who are possessed of great mental activity and spontaneity, and also those who in ordinary life give the impression of being "nervous," show a greater tendency to contract the disease than those of phlegmatic disposition. Individuals whose feelings and thoughts are greatly disturbed by every insignificant occurrence are found with proportionate frequency among the sufferers from diabetes. There are many carefully observed cases on record in which a speedy outbreak of the disease followed a sudden fright or joy or some other occurrence causing a disturbance of the mental equilibrium.

IX. Other Diseases.

1. *Infectious Diseases.*—It has often been sought to establish some connection between diabetes and other diseases, and indeed there is hardly a disease which has not at some time or other been looked upon as the exciting cause of this affection. In most of these cases the causal relation between the two diseases is very doubtful, furnishing an instance of the confusion of *post hoc* and *propter hoc*. I cannot refrain from relating a characteristic example of this kind. I was called to see a patient with diabetes who told me that his trouble was the result of a severe attack of influenza. While under treatment for the influenza his urine was examined for albumin and sugar; the former was present in small amount, the latter was absent. After the influenza had subsided the quantity of urine excreted became greatly increased, and another examination showed the presence of sugar. Since that time the glycosuria had persisted. Soon after this I received for examination the statement of a life insurance examiner concerning this patient. The man had applied for insurance prior to the attack of influenza, and an examination of the urine made at that time showed that it contained sugar. In this case, as so often happens, the intercurrence of an infectious febrile disease temporarily interrupted the glycosuria. The patient's statement was made in perfectly good faith, for he had not been informed of the discovery of sugar in his urine before the attack of influenza. A similar ex-

planation may well be imagined for many cases in which diabetes is said to have followed an attack of acute infectious disease. We may assume that not infrequently the disease was present prior to the attack, but that the symptoms were so slight as to pass unobserved, no mention of them being made to the family physician. But after an intercurrent attack of some infectious disease the patient feels weak and convalescence is slow, the urine is examined and a diagnosis of diabetes is established.

But it cannot be denied that acute infectious diseases may actually cause diabetes. Observations made during the past few years, which have taught us to recognize a certain form of diabetes as an organic disease (pancreatic diabetes), have made this relationship more explicable. We so often observe organic affections (involving the heart, kidneys, liver, nerves, etc.) occurring as sequelæ of acute infectious diseases, that we may also regard a secondary affection of the pancreas as altogether possible and even probable. There is a wide field here for more exact observations.

Equally uncertain are the reports alleged of the occurrence of diabetes after severe hemorrhages, frequent child-bearing, extensive eczema and other skin eruptions. We have reports for the most part of isolated cases only, the value of which as a basis for generalization concerning any disease is very slight.

Worthy of more especial consideration as etiological factors are obesity, gout, nervous diseases, diseases of the pancreas, and syphilis.

2. *Obesity.*—That diabetes and obesity are frequently associated is an old-established fact. It almost always happens that the obesity comes on first and exists for a number of years before sugar appears in the urine. It is usually, therefore, not until after the fortieth year that the sugar first begins to be excreted. The diabetes associated with obesity is commonly of a benign nature, and a slight glycosuria may exist for years or even decades without affecting the patient's powers to any appreciable degree. It may even disappear completely, for instance after the institution of a suitable diabetic regimen, but returns again if the patient grows lax in his observance of the prescribed mode of living.

Much more unfavorable are those cases in which both obesity and diabetes are developed in early life. Under such conditions one may see an herculean frame, both fat and strong in muscle, admired for its powerful proportions, waste away and become reduced to a mere skeleton in a few months.

The following figures give an idea of the frequency of the coincidence of diabetes and obesity: Frerichs had 59 cases of obesity among 400 diabetic patients, or 15 per cent., Seegen 30 per cent.,

and Bouchard 45 per cent. It has been remarked by some (Bouchard, Kisch) that in families in which obesity is common, one or another member who is himself not obese suffers from diabetes. Of Bouchard's patients 36 per cent. gave a history of obesity among their ancestors.

In the treatises on diabetes in the text-books the view is generally held that diabetes occurs secondarily to obesity, and this form of the disease is therefore designated as "lipogenous diabetes." Kisch in particular holds to this view. Others express themselves with great reserve concerning the exact relation existing between the two affections, although admitting the fact of such relation. Seegen believes that obesity is frequently a precursor of diabetes. I myself have already expressed the opinion, in my work on "The Pathology of Metabolism," that our present knowledge of the mutual relations of carbohydrate and fat exchange permits of a more profound understanding of the interdependence of diabetes and obesity than is ordinarily admitted. I have already laid stress upon the belief that, in every case of true diabetes, not only the exudation of carbohydrates but also their conversion into fat must be restricted. Were the first-named function alone interfered with there could be no long-continued and excessive glycosuria, especially if the diet were one poor in carbohydrates, so that the entire amount of sugar thrown into the circulation would be comparatively small and very much below that ordinarily taken up from the intestinal canal of a healthy man living upon an unrestricted mixed diet. In such a case the carbohydrates not consumed in the muscles, glands, etc., would be seized upon by the fat-forming cells and, through welding together of the molecules, be compressed into fat, just as occurs in the healthy organism. Hyperglycæmia and glycosuria can follow only when the fat-forming as well as the oxidizing cells have lost their power of arresting the sugar molecule. It is possible that both the consumption (oxidation) and the storage (fat conversion) of the material are interfered with by a common cause, as for example the resistance of the diabetic tissues to glycogen formation, but on this point we have as yet no certain knowledge.

The following consideration seems to me to be justified by what has just gone before. It may be conceived that there are cases in which at first the power to burn up sugar in the organism is alone interfered with, while the conversion of carbohydrates into fat still goes on. Under these circumstances the working cells of the body are richly bathed in a nutritive sugar solution; nevertheless they are starved because they cannot, or at least can only with difficulty, seize upon the sugar molecule. As a consequence of this there occurs a

sort of tissue hunger which excites reflexly a sharper appetite and leads to the ingestion of a greater quantity of food. The latter results directly in an increased deposit of fat. Such individuals are diabetic, only they do not excrete sugar externally through the urine but rather into the freely accessible layer of adipose tissue. The adiposis masks the diabetes; we have to do, in fact, with a "diabetogenous obesity," as I call the condition in opposition to the common teaching of a "lipogenous diabetes."

A logical analysis leads us to the following schema:

a. There are cases in which the consumption of sugar and its conversion into fat are simultaneously restricted—glycosuria of varying degrees of gravity and emaciation (ordinary diabetes).

b. There are cases in which only the burning up of sugar, and not its conversion into fat, is interfered with,—obesity without glycosuria (masked diabetes); these pass readily at a later period into

c. Cases in which the consumption of sugar is restricted and the heaping up of carbohydrates in the fatty tissues is also more or less interfered with—obesity with consecutive glycosuria (ordinary diabetes of the adipose).

I regard this theory as by no means filling all the gaps existing in the present state of our knowledge, but I think that the teaching as far as it goes is warranted. The fact of a relationship between diabetes and obesity is, in the light of my theory, no longer questionable, but follows logically from the connection which has been found in recent years to exist between carbohydrate metabolism and fat formation. It may, indeed, be said that, even if practice had not long since spoken correctly, theory would have forced us to construct an hypothetical relationship between diabetes and obesity.

3. *Gout.*—The frequent coincidence of gout and diabetes has been often remarked upon. In Germany, where gout is not common, the opportunity for observations of this kind is not often presented, and it is, therefore, not to be wondered at that we have to look for illustrations of this relationship to English and French authors especially. Their writings are rich in observation of this kind. Among Englishmen, Prout, Bence Jones, Lauder Brunton and Sir Dyce Duckworth have especially emphasised this point; of the French writers we may mention Claude Bernard, Brongniart, Charcot, Bouchardat and Bouchard.

The connection declares itself in various ways. Often typical gout occurs in middle life; later the attacks cease and glycosuria appears. Again cases are observed in which attacks of gout alternate with glycosuria (diabetes alternans). In a third group gouty symptoms and glycosuria are present at the same time. Most of the cases

of this kind reported were of slight gravity, interfering little or not at all with nutrition, and not incompatible with a long life. Less benign were those in which diabetes existed first, the gouty symptoms appearing later (Bouchardat).

It has been previously remarked that sufferers from diabetes not uncommonly present an ancestral history of gout (hereditary alternating gout).

An insight into the intimate relation between gout and diabetes has not been vouchsafed us. Our knowledge on this point is much less certain than on the connection between obesity and diabetes, and very naturally, since we know almost nothing of the true nature of gout. We are ignorant of the chemical processes which lead to an increased formation and excretion of uric acid, and the many tomes which have been written on this subject contain only the smallest fragments of real knowledge, the rest being pure hypothesis. Any further study of the intimate connection existing between diabetes and gout would therefore be unprofitable.

4. *Nervous Diseases.*—Diabetes is so often observed in individuals suffering from disease of the nervous system that a relationship of cause and effect cannot be gainsaid, but there is much discrepancy among writers as to the extent to which this relationship exists. Naturally every anomaly of the nervous system in diabetics is not to be regarded as the exciting cause of the glycosuria; for commonly enough the case is reversed, diabetes being the primary, and the nervous affection (for example neuralgia, neuritis, or neurasthenia) the secondary condition. But even when this is carefully kept in view, every physician who has had many cases of diabetes in his practice can call to mind a number of instances in which the diabetes has made its appearance during the course of some nervous malady.

But when we go further and attempt to trace a connection between diabetes and any special lesions of the nervous system, we tread at once upon uncertain ground. There is little that can be said on this point. Glycosuria, as a chronic affection, follows cerebral lesions much more frequently than it does spinal or peripheral alteration. Among functional nervous diseases neurasthenia leads in an etiological sense, hysteria being far behind. Diabetes occurs also in the insane, yet the statistics of asylums show a smaller percentage of diabetics than do those of general hospitals. From a comparison of the statistics of the Charité Hospital in Berlin I gather the following: During the years 1890–1893, 23,825 patients were treated in the four medical divisions, among whom were 67 diabetics, or one diabetic for every 355 patients; during the same period, in the psychiatric clinic of the Charité, out of 2,535 patients not one suffering from

diabetes was found. These figures are large enough to deserve attention.

If now we turn from this general survey to a consideration of the more important details, we find most worthy of note those cases in which diabetes has followed immediately upon an injury or concussion of the brain. Cases of this kind are always most striking and belong to those against which objections can least often be urged. As regards the clinical forms of the disease so occurring, we find every grade of transition, from an insignificant glycosuria lasting only a few days or hours up to a disease presenting a complete picture of chronic diabetes mellitus.

We are fortunately in position to arrive, through the results of experiments, at an understanding of those cases of *temporary* glycosuria which follow an acute brain injury, whether this have been produced by external violence, by intracranial embolism, or by rupture of a vessel. We must recall Claude Bernard's *piqûre*, and also the fact that the same result has been observed to follow other acute injuries of the most varied character to the nervous system in animals. The reference to these experimental results is certainly justifiable, and all authors admit it. We have to assume that a centrifugal irritation passes from the injured portions of the central nervous system to the liver, causing this organ to give up its stores of glycogen. As then the consumption of sugar does not keep pace with the over-saturation of the blood, acute temporary hyperglycæmia and glycosuria result.

Possibly now we are also warranted in assuming that, following upon a sudden injury of this sort, a permanent irritation proceeds, directly or reflexly, under certain circumstances from the organically injured or functionally diseased portions of the nervous system, and is transmitted to the glycogen-storing organs (muscles, liver, and other glands) and these exert a continuous opposing influence to the accumulation of glycogen. This disturbance leads further to hyperglycæmia and glycosuria.

I must not neglect to mention that the participation of the pancreas is alleged even in neurogenous diabetes. In accordance with this doctrine we must assume that influences of either a restricting or a stimulating character are reflexly transmitted to the pancreas from the diseased nervous area, and these cause a disturbance of function. Opposed to this conception, however, is the fact that even in the most marked lesions of the nervous plexus surrounding the pancreas, only transitory glycosuria at the most, never permanent diabetes, is produced. This objection is, of course, not absolutely conclusive, but all explanations of what actually takes place in neurogenous diabetes must be regarded as yet as purely theoretical.

F. A. Hoffmann[11] has endeavored, from the study of a rich collection of clinical material, to form a picture of the peculiarities of neurogenous diabetes. In this form of diabetes, he maintains, obesity is never developed. He gives further the following differential table:

Neurogenous Diabetes.	Diabetes of the Obese.
Occurs with preponderating frequency in men.	Occurs as frequently in women as in men.
There is no tendency to the formation of furuncles, carbuncles, or cataract.	There is a strong tendency to such formations.
Has no connection with gout.	Is often connected with gout.
Passes away if the brain affection is curable, and then always in a comparatively short time. In other cases it causes death within two years.	Is very chronic, often lasting ten or twenty years.

5. *Disease of the Pancreas.*—Since the wonderful discoveries of von Mering and Minkowski particular attention has very naturally been directed, in the study of diabetes, to the pancreas. But it would be belittling the services of earlier investigators not to mention the fact that the importance of pancreatic disease in the etiology of diabetes was signalized a hundred years ago by Cawley, and since his time by many other writers (for example, Bouchardat, Friedreich, Bamberger, Frerichs, Senator, and Seegen). Still, these observations were little more than reports of cases, and an opinion as to the causal relation present was never clearly formulated until Lancereaux, in 1877, on the strength of numerous clinical and anatomical observations, described a special form of diabetes under the name of *diabète pancréatique ou diabète maigre.* This form was said to be characterized by a sudden onset, unusual malignancy of course, rapidly progressive emaciation, rapid loss of strength, and a special tendency to pulmonary tuberculosis as a complication. Lancereaux's cases, which were reported at length by Lapierre in his Thèse de Paris, had excited a good deal of well-deserved notice among clinicians, but were on the point of being forgotten again when the discovery of experimentally induced pancreatic diabetes revived a recollection of them and bore striking witness to the clinical acumen of Lancereaux. Since then the number of cases reported of diabetes associated with diseases of the pancreas has assumed considerable proportions. An explanation of the mode of origin of diabetes in disease of the pancreas cannot be again entered upon here, as it has already been treated of at length elsewhere (pp. 54, 58, 70).

In the light of our present knowledge based upon the facts of experimental pathology and clinical experience, the existence of pancreatic diabetes can no longer be doubted, although it may still be

questionable whether the clinical picture drawn by Lancereaux is correct in all its details. It will be the task of clinical medicine to complete this picture and to correct its defects. We may then hope to gain such an insight into this condition as to be able to diagnose *intra vitam* the disease of the pancreas which holds an etiological relation to diabetes, or in other cases to exclude it. A noteworthy beginning has already been made in this direction, but in the mean while we cannot ignore the fact that many obstacles are still to be overcome before we establish satisfactorily the doctrine of pancreatic diabetes in man. In the first place, there are numerous cases on record in which extensive lesions of the pancreas have been found post mortem, although during life there was no glycosuria (see the monograph of I. Seitz on Necrosis of the Pancreas). Then there are also very many cases of diabetes reported in which the most careful examination of the pancreas has failed to bring to light the existence of any lesions in this organ. Some authors go so far in these cases as to inculpate the pancreas in spite of the absence of any anatomical lesion, alleging in support of their view the indubitable fact that an organ may be functionally diseased although all our known methods of research are unable to detect any anatomical basis therefor. This assumption is based upon the attempt to explain all cases of diabetes from one uniform standpoint, viz., that an alteration of the pancreas must always either be the primary cause of diabetes or else it must act as the necessary connecting link between some remote cause and the outbreak of the disease (see above, in the section on Neurogenous Diabetes).

This argument manifestly goes too far. It cannot, indeed, be positively disproved, but neither can it be established as correct; yet men take it into regions of utter darkness where the door is flung wide open to the most boundless and inconsequential speculations. If, at this early period, we attempt to bring every case of diabetes into relations with the pancreas, we run the risk of impeding the healthy development of our knowledge concerning the disease, just as it was at one time restricted by a one-sided view of the action of the liver in the causation of diabetes. It is still necessary, bearing well in mind what has already been accomplished, to collect and critically sift a great many more clinical and pathological facts before we can arrive at any certainty.

6. *Syphilis.*—A few words must be said concerning the relation of syphilis to diabetes. It cannot be denied that evidences of syphilis have been found, either during life or post mortem, in very many cases of diabetes, a fact that, in view of the wide dissemination of syphilis, need excite no wonder. Isolated cases of diabetes have

very often in times past been referred to syphilis for their exciting cause. They were cases in which disease of the cerebral arteries and of the brain itself had been caused by the action of the syphilitic poison, and if it be admitted that diabetes may be produced by influences emanating from the central nervous system it follows as a consequence that diabetes may stand in immediate causal relation to syphilis. This assumption has an important therapeutic aspect in view of the fact that neurogenous diabetes is most frequently curable and disappears coincidently with the subsidence of the cerebral affection.

Furthermore, it is certainly of importance, in this connection, to examine into diseases of the pancreas of syphilitic origin. Among all the changes of the pancreas leading to the production of diabetes simple atrophy and sclerosis (overgrowth of the connective tissue at the expense of the parenchyma) seem to be the most frequent. It has not yet been decided how far these diseases may be caused by syphilis, either directly or as a result of an intervening endarteritis. The determination of this question is also of importance in a therapeutic sense.

On the other hand it is going decidedly too far to assert flatly, as some authors do, that diabetes is a syphilitic disease. This theory is advocated by Schnee in his monograph on Diabetes. He holds that all cases of diabetes are referable to an hereditary predisposition, indeed that they are all associated with hereditary syphilis. Such a view must be absolutely rejected, for it is altogether insufficient and is opposed by the results of a careful analysis of all the anamnestic points in numerous, I might say most, cases of diabetes. More than that, it may be remembered that diabetes was a disease recognized by Greek and Roman physicians, while syphilis is supposed to have been communicated to Europeans by the Indians, after the discovery of America, as if in revenge for their discovery and annihilation (C. Binz[13]).

CHEMICAL PATHOLOGY AND METABOLISM IN DIABETES.

I. The Glycosuria.

Glycosuria stands out most prominently among all the symptoms of diabetes. We have already seen that "diabetes mellitus" and "glycosuria" are not notionally coincident. The first term is employed to denote the disease in its entirety, the second to express a phenomenon consequent upon an unknown process concerning the true nature of which our knowledge is as yet purely hypothetical.

For the physician, however, glycosuria is more than a symptom in the ordinary meaning of the word. It is for him in every case the object of special study and in every case the object of therapeutic consideration. In many, I might say in most, of the measures taken the physician thinks more of repressing the glycosuria than of removing the diabetic diathesis. He is right in so acting, for in so far as he contends against the symptom which is amenable to treatment he helps the patient; he takes away from the disease a weapon with which it threatens life. In order to be able to do this with success, while avoiding the attaching of undue importance to the symptom, a clear insight into the symptomatic forms of glycosuria and the metabolic significance of this phenomenon is necessary.

1. *The Daily Amount of Sugar Excreted, and its Estimation.*

The amount of sugar excreted varies greatly in different cases and also at different times in the course of the same case. Some diabetics excrete only a few grams daily or even none at all, while in others the quantity of sugar passed in the urine in the twenty-four hours may amount almost to a kilogram (two pounds avoirdupois). Such excessive figures are, however, very rarely met with, although a daily excretion of from 300 to 500 grams (one-half to one pound) is not uncommon.

It is important to know the total amount excreted in a given case. To determine this the patient must be instructed to save all the urine passed in the twenty-four hours in a common receptacle. This quantity is carefully measured, and then a sample is subjected to a quantitative analysis for sugar. It is very important to mix together all that is passed in the twenty-four hours, since the amount of sugar may vary considerably in the single portions voided at different times of the day.

After the percentage of sugar has been determined and the total amount of urine passed has been measured, we have still not done much to aid us in judging of the gravity of the case. We often hear the laity and even physicians express themselves somewhat as follows: "As regards the patient X matters are not so bad, for he excretes only 2 per cent. of sugar in the urine; but Y has a very grave form of diabetes, for he always has 6 per cent. or more of sugar in his urine;" or similar comparisons are made concerning the daily amounts excreted, as, for example, a case with a daily excretion of 50 grams is regarded without further consideration as less severe than one whose urine contains 250 grams in the twenty-four hours. Comparisons of this kind are justified only when the diet in the given cases is exactly the same, but they are utterly worthless and misleading

when the food of the two patients varies in quantity and quality. When the nature of the diet is taken into consideration it may well be that the disease will be found to be actually much more grave in the patient who excretes the daily amount of only 50 grams than in the one who passes 250 grams. This would be true, for example, if the first patient carefully avoided the ingestion of food containing carbohydrates, while the second indulged freely in articles rich in these substances.

2. *The Various Degrees of Glycosuria and their Oscillations.*

The question that has always to be determined in judging of a given case is: To what extent is the individual able to consume carbohydrates in his body? We have seen that the healthy man is fully prepared to deal with very large quantities of carbohydrates by (1) burning a part at once, thereby meeting the requirements of heat production and labor, (2) storing up a second portion in the form of glycogen, (3) slowly converting another portion into fat, and (4) excreting a fourth, very small, part in the urine, in cases in which carbohydrates have been ingested in unduly large amounts and at short intervals. Now in a diabetic the first three of these modes of sugar disposal are in some way interfered with, and the extent of the fourth serves as a measure of the degree of this interference. The more of a given quantity of sugar, introduced into the organism for purposes of estimation, that appears again in the urine, the more pronounced will the interference with the consumption of sugar be regarded. Naturally, in order to find the degree in which the sugar excretion occurs, we must have a standard measure which we can use as a basis for our calculations.

A procedure which was suggested independently of each other by I. Seegen and M. Traube, and which has been found to answer the purpose admirably in practice, is the following: The condition of the urine, when the patient is on a diet absolutely free from carbohydrates, is first ascertained. According as it is then free from sugar or not, a distinction is made between mild and severe cases. I prefer to use the term mild and severe glycosuria.

a. Mild Glycosuria.—This is characterized by the fact that the urine becomes sugar-free within a few days after all carbohydrates have been withdrawn from the diet, and only when the carbohydrates are again ingested does sugar reappear in the urine. Let us understand clearly the conditions present. Even when carbohydrates are withdrawn from the diet the organism is by no means sugar-free. Sugar is continually formed from the albumin and, as I believe, under certain circumstances from fat as well. But all these carbohydrates,

set free in the body during regressive metamorphosis of highly constituted molecules, are formed very slowly, and a sudden flooding of the organism with carbohydrates can never occur in this way. If the diabetic's power of consuming carbohydrates is only moderately restricted, the organism is well able to dispose of these slowly formed quanta of grape sugar and excretes none in the urine.

These "mild cases" present every form of gradation. Some patients are free from glycosuria only when the food contains absolutely no sugar; others again may take carbohydrates in small quantities, perhaps 40 to 60 grams in divided doses throughout the day, without becoming glycosuric, but if they should take this amount at one dose, they would immediately pass a portion of it in the urine. The mechanism of this is easily understood: the organs are capable of attending to the carbohydrates passing into the circulation slowly a little at a time, but are unable to cope with them when suddenly introduced in quantity. In other patients we can give with safety still larger amounts, 100 to 150 grams of carbohydrates being easily disposed of, sugar appearing in the urine only when this limit is exceeded.

In order to obtain comparable values I always start with the same fixed diet—a standard diet. Before the patient is finally put upon it I prescribe a gradual reduction of carbohydrates, not shutting them off suddenly and entirely. My standard diet, in which in the case of the poor I substitute other cheaper articles but of the same nutritive values, is the following:

Breakfast: 5 gm. of tea steeped in 200 c.c. of water; 150 gm. of ham; one egg.

Lunch: 200 gm. cold roast beef; 60 gm. fresh cucumber with 5 gm. vinegar, 10 gm. olive oil, and salt and pepper to taste; 20 c.c. brandy with 400 c.c. Apollinaris water; 60 c.c. coffee without milk or sugar.

Dinner: 200 c.c. clear bouillon; 250 gm. beef (weighed raw) basted with 10 gm. butter; 80 gm. green salad, with 10 gm. vinegar and 20 gm. olive oil, or 3 tablespoonfuls of some well-cooked green vegetable; 3 sardines à l'huile; 20 c.c. cognac with 400 c.c. Apollinaris water.

Supper: 2 eggs (raw or cooked); 400 c.c. seltzer water.

This standard diet is free from carbohydrates; it contains very nearly 200 gm. albumin (with 32 gm. nitrogen) and about 135 gm. fat. As soon as the urine has been free from sugar for two or three days under this diet, gradually increasing amounts of starch up to 20, 50 and 100 gm. are added. I sometimes give for this purpose white bread, containing 55 per cent. of starch, and sometimes Albert

biscuit which contains 75 per cent. of starch. As soon as, under these increasing additions of starch, sugar reappears in the urine, we get the formula:

Tolerance = standard diet + x gm. starch.

In patients with mild glycosuria a careful observer can convince himself most positively that the diabetic disturbance is not constantly the same in a given case, but that it oscillates in a remarkable and wholly unaccountable manner, and indeed—a fact which I wish especially to emphasize—independently of any therapeutic interference. As an example of this I recall the case of a corpulent patient with diabetes whom I had under observation for a number of years; at first he could take 5 gm. of starch daily without excreting sugar in the urine; a few months later the tolerance had risen to 80 gm., then fell back to 20 gm., and afterward rose again to 100 and even 150 gm. of starch. Frequently the oscillations are even much more marked. There are patients who for a long time can bear almost no carbohydrates; then the glycosuria entirely subsides, sometimes gradually, at other times tolerably quickly, and the individuals may go to the family table and eat the ordinary diet there offered without showing a trace of sugar in the urine; and then at a later period, months or years afterward, the glycosuria reappears. Observations of this kind are especially frequent in corpulent or gouty persons.

In cases of this kind it often seems as though the therapeutic measures instituted, for example, a course of the waters at Kissingen, Carlsbad or Neuenahr, had had a very positively favorable influence. In other instances a much less marked interference with the patient's mode of living appears to effect a change for the better; such may be increased muscular exercise, the disuse of alcohol or tobacco, insistance upon a regular action of the bowels, and the like. We shall speak of this again in the section on the Treatment of Diabetes, and only refer to it here as a warning against an overestimation of the value of such measures. It is indeed often very difficult for the physician, who has a modest appreciation of his own powers and of his success in therapeutics, to decide, in this disease, whether he is in the presence of a spontaneous improvement or of one brought about by medical art.

b. Severe Glycosuria.—This is characterized by the fact that the excretion of sugar continues in spite of the total withholding for days of carbohydrates from the diet. It signifies that even the carbohydrates gradually and slowly formed from the albumin, and admitted a little at a time into the circulation, are not wholly consumed. The functions of glycogen storage, of the splitting up of the sugar

molecule in the tissues and of its compression into fat must be very seriously affected.

Here also there are many degrees of gravity, the tolerance of carbohydrates varying greatly in different cases. Some diabetics, for example, with a daily ingestion of 1,000 gm. of meat will still continue to excrete sugar, but if the amount is reduced to 500 gm. the glycosuria ceases. What is the significance of this phenomenon? In 1,000 gm. of flesh-meat there are about 212 gm. of albumin, in 500 gm. about 106 gm. of albumin. Now it is known that the decomposition of albumin in man keeps pace nearly with its ingestion; and this holds true in the main even in diabetics. Therefore, after the ingestion of 1,000 gm. very nearly, although not exactly, a double quantity of albumin is decomposed in the body, and therefore also approximately double the amount of carbohydrate is formed by the division of the albumin molecule. In our supposed case the quantity of sugar formed from 500 gm. of meat was disposed of in the body, but that formed from 1,000 gm. of meat could not be entirely consumed. In the severest, but very rare, cases, the urine does not become sugar-free even when the decomposition of albumin is reduced to its lowest possible figure, that is, during an absolute fast.

For the estimation of these severe forms of glycosuria the above-described carbohydrate-free standard diet is also suitable; the more sugar that remains in the urine after the institution of this diet the more grave is the glycosuria. If such trials are repeated from time to time it will be found that, in these severe forms as well as in the milder ones, the sugar-destroying power varies in energy in individual cases. Cases will frequently be encountered in which sugar disappears from the urine immediately upon the institution of the standard diet, which respond at once to any addition of carbohydrates although they bear very well an increase in the amount of albumin (transition forms; see below). These cases are more favorable than those in which sugar continues even with the standard diet, but are less favorable than those which can bear a slight addition of carbohydrates to this standard diet.

c. Critical Remarks concerning the Division into Severe and Mild Forms of Glycosuria.—Most authors believe that the difference between severe and mild forms of glycosuria is merely a quantitative one. I am also of this opinion, but there are those who hold the contrary. Among the most prominent of the latter may be mentioned I. Seegen, who has endeavored in numerous writings to prove that these two forms constitute distinct diseases. The mild form is referred to disease of the liver, the severe form to a functional disturbance of all the cells of the body. In the mild form, says Seegen,

only the nutritive sugar, but in severe forms that also which is produced in the liver from albumin ("liver sugar") is excreted in the urine. The first is only fat forming, the second is fuel for consumption in the body.

The following may be said against this division and the theoretical grounds upon which it is made:

1. We know of no physiological fact upon the strength of which it may be assumed that the sugar ingested with the food finds any application essentially different from that of the sugar formed within the body itself. But, on the contrary, we know of many facts which prove the opposite, especially the facts of the mutual interchangeability of nutrient material according to the laws of isodynamia.

2. Between the mild and severe forms of glycosuria we meet with transitional forms. A glycosuria which is at first mild may often become severe, although the reverse is rare. Neither pathologically nor etiologically, nor in respect to complications and final outcome, can any essential difference be justly maintained. On the contrary, experiment has shown that, after a lesion of the pancreas, at first a mild form of diabetes occurs, and later, as the pancreatic affection continues and passes into atrophy of the organ, the diabetes merges into the severe form (Sandmeyer[8]); this speaks in the strongest manner in favor of the unity of the cause and of the merely quantitative difference in degree of the two forms. As regards prognosis there is, it is true, a difference. This is comparable to the difference existing between a very chronic pulmonary tuberculosis accompanied with marked new connective-tissue formation and an acute caseous pulmonary phthisis. Both are essentially the same disease, yet how different in course and prognosis!

3. We must indeed admit the fact, adduced by Seegen, that the carbohydrates of the food are much more likely to cause glycosuria than those formed in the body from albuminates. It is very clearly seen in the transitional forms. Still it is not permissible to conclude from this that there is any qualitative difference in the uses to which the carbohydrates derived from these two sources are put. The difference remains always a quantitative one and can be explained in the following way:

a. The rapidity with which the sugar introduced through the mouth enters the blood is much greater than that with which sugar is formed from the slowly absorbed and slowly decomposed albumin. The cells are able to take care of the sugar coming to them gradually, but not of that suddenly poured upon them.

b. The sugar derived from the food reaches the cells as a ready-formed molecule (grape sugar) and approaches them from without;

the sugar derived from albumin originates in the cells themselves and presents itself to their uses in the nascent state. It is easy to understand that the cells may be fully capable of disposing of the nascent molecule while unable to cope with one already formed.

3. *Directions for Measuring the Intensity of the Glycosuria.*

If it is correct to say that a hard and fast line between "mild" and "severe" forms of diabetes cannot be drawn, then practical necessity only prescribes with what measure we shall estimate the degree of disturbance of the sugar-consuming function. The procedure above described answers all practical needs and has the advantage of pointing out a secure path for the therapy of the disease. For the sake of a better apprehension of the subject I will briefly state once more the measures to be employed. These are:

a. For a few days, gradual withdrawal of carbohydrates from the food.

b. For five days, the standard diet (p. 76).

c. If the urine now becomes sugar-free, a progressively increasing quantity of starch is added to the standard diet until glycosuria returns. The tolerance is expressed by the formula:

$$\text{Tolerance} = \text{standard diet} + x \text{ gm. starch.}$$

d. If, while the patient is on the standard diet, the sugar disappears from the urine but returns immediately upon the addition of a small amount of carbohydrate, then 100 gm. of meat may be added. The addition of a larger quantity is unnecessary, as it cannot be utilized in practice. In general this test has more of a theoretical than a practical value, and may therefore be omitted. The formula reads:

$$\text{Tolerance} = \text{standard diet} + 0 \text{ gm. starch.}$$
$$= \text{standard diet} + 100 \text{ gm. flesh meat.}$$

e. If the glycosuria continues after the patient has been put on the standard diet, the amount of sugar in the urine is to be determined, its average from the third to the fifth day of the standard diet being estimated, and the condition is then indicated by the formula:

$$\text{Tolerance} < \text{standard diet; sugar} = x \text{ gm.}$$

By means of this method, which demands only simple and easily executed analyses, the physician may arrive at the most exact appreciation of the intensity of the disturbance causing the glycosuria. He can without any further investigation compare one case with another and gather definite data concerning the progress of any given case; temporary improvement or exacerbation will not escape him, and he can accurately estimate the results of dietetic or medicinal treatment.

Besides this method, which always demands a certain control of the patient and can therefore be carried out only in hospitals or private clinics, the following procedure has stood me in good stead:

I order a diet which is poor in carbohydrates, but permit no trace of carbohydrates to be ingested after three o'clock in the afternoon. On the following morning the patient, on rising, voids the night urine, and then preserves that passed two hours later, without in the mean while having taken anything to eat or drink. This urine is brought to the physician and examined. Frequently this urine, excreted while the patient is fasting, contains no sugar at all; at other times the variations in the amount of sugar contained in it enable us to judge of oscillations in the intensity of the disease. The advantage of the method consists in this, that a sample of urine is examined the composition of which is scarcely influenced by the quality of the food ingested (*urina sanguinis autorum*).

It is hardly necessary to utter the warning not to confine the examination ordinarily to samples of urine excreted only during the morning hours, for were that the rule many cases of diabetes would never be diagnosed at all.

4. *Dependence of the Glycosuria upon the Kind of Carbohydrates Ingested.*[14]

Wherever exhaustive researches have been instituted it has always been found that no case of diabetes in man is so severe that all the carbohydrates ingested are excreted again unconsumed (Külz, Leo, and others). Furthermore it has been shown, as was discovered by Külz and confirmed later by C. von Voit, F. Voit, von Noorden, Minkowski, S. Solis Cohen, Saundby, Bohland, and others, that the diabetic organism is not impotent in equal degree in the presence of all kinds of carbohydrates.

If equal weights of different kinds of carbohydrates are administered in succession, the diet otherwise remaining the same, it is found that—

Grape sugar (dextrose, glucose) raises the percentage of sugar in the urine to the highest point and the most quickly.

Starch and other carbohydrates (such as maltose and dextrin) which, either in the digestive tract or immediately after their absorption, are converted into grape sugar, approach grape sugar very closely in this respect.

Fruit sugar (levulose) increases the glycosuria to only half the extent, or even less, that grape sugar does.

Milk sugar and cane sugar occupy a middle place, in their glycosuric action, between grape sugar and levulose.

The fact that the diabetic organism disposes of some sorts of sugar molecules better than of others is both theoretically and practically important, because—

a. It is incomprehensible on the theory of an "over-production of sugar," but is easily explicable on the theory of a "diminished consumption of sugar." It finds its analogue in the decomposition of carbohydrates by certain vegetable cells. For example, the common yeast fungus (Saccharomyces apiculatus) seizes upon grape sugar and fruit sugar and converts them into alcohol and carbonic acid, but it has no power over cane sugar, milk sugar, or other varieties.

b. It is worthy of remark that levulose is comparatively well borne by diabetics. It is after the ingestion of this special form of sugar by diabetic animals that large amounts of glycogen are stored up in the liver, while the organ remains free from the substance after the ingestion of grape sugar and starch.

c. It is important as regards the nourishment of sufferers from diabetes that some variety of carbohydrate should be known which is not as readily excreted unchanged through the kidneys, but which, through its consumption in the body, assists in the production of heat and force.

5. *Relation of Glycosuria to the Ingestion of Fat and Alcohol.*[15]

a. Fat.—Up to the present time the influence of carbohydrates and albumin upon the excretion of sugar has alone entered into consideration. But it is of the utmost importance to know how fat acts in this respect. Fat is an invaluable nutrient material for the diabetic—it is his sheet-anchor. This is owing, in the first place, to its high nutritive value, and secondly to the fact that its ingestion never increases the glycosuria. This observation has been often made in cases of diabetes by Cantani, Ebstein, von Mering, F. Hirschfeld, Weintraud, and others, and has also been noted in experimental diabetes following extirpation of the pancreas and in phloridzin poisoning.

b. Alcohol.—The use of alcohol is recommended in almost all treatises on diabetes. But caution in this respect is necessary, and one should never exceed the use of moderate amounts, observing carefully the influence of the alcohol upon the glycosuria and upon the general condition of the patient. Increase of glycosuria after the ingestion of alcohol has been noted only by some of the older writers, and their conclusions are based upon inexact observations. Külz has made a study of this point, and has never seen any bad results follow the drinking by diabetics of one bottle daily of some strong

dry wine; in one carefully studied case of this sort, the glycosuria even fell. I myself have often seen either no effect or a slight improvement, but have never observed any appreciable increase in the glycosuria when the use of alcohol was kept within moderate limits. For a further discussion of the effects of alcohol the reader is referred to the section on Treatment.

6. *Relation of Glycosuria to Muscular Exercise.*[16]

As a general rule the effect of muscular exercise is to reduce the glycosuria, the dietary condition remaining unchanged (Zimmer, Külz, von Mering). Among the exercises of this nature are walking, mountain-climbing, wheel-turning, work at the ergostat, etc. This fact is readily understood, if we remember that in health the muscles supply their needs of heat and force production by means of carbohydrates, and that muscular activity increases greatly the consumption of this fuel. A portion of the grape sugar which would otherwise have escaped in the urine is taken up by the muscles. Finkler has observed that massage of the muscles acts in the same way as active exercise.

A decrease in the glycosuria is not always, however, brought about by muscular exercise. Külz has noted exceptions to this rule, even the opposite effect. If, in a given case, glycosuria increases in consequence of work it may be assumed that it is the result of an unusual fatigue felt by the patient during or after his exercise. In such a case, the extra demand is evidently met by the consumption of other substances, probably albumin, and the increased destruction of albumin in turn leads to an augmented sugar excretion. Whether other influences, possibly reflex nervous irritation, also take part in paralyzing the sugar-consuming function, cannot be safely predicted.

A diminution in the glycosuria following muscular labor is usually observed in recent cases, in which the nutrition is still well sustained; an increase of the process from the same cause is seen in old cases and in greatly emaciated individuals.

7. *Relation of Glycosuria to the Condition of the Nervous System.*

All diabetic patients react to psychic and mental disturbances very badly, being greatly fatigued and exhausted by them. This effect, however, varies within wide limits according to the individual resisting power of the patient, and stands in no direct relation to the intensity of the glycosuria.

In many cases the relation of the glycosuria to the condition of the nervous system stands out very sharply. Every physician can recall cases in which mental excitement of any kind, or an unwonted

intellectual strain, has been followed by a series of sleepless nights, or in which an irritation of the nervous system through bodily pain has resulted in a marked and permanent depression of the tolerance for carbohydrates. Observations of this sort may be made in every form of diabetes, whatever its cause may be and whatever its degree of mildness or severity.

8. *Relation of Glycosuria to the Condition of the Digestive Organs.*

In diabetes the paradox has been observed that the glycosuria—the phenomenon upon which we depend especially to measure the gravity of the disease—diminishes immediately upon the intercurrence of gastro-intestinal disturbances. This is, however, only an apparent paradox, and its explanation is simple. In the first place, all gastro-intestinal disturbances of whatever nature are associated with loss of appetite, and with the cutting off of nutritive material the most productive source of the urine sugar begins to flow less freely. In other cases the same result follows, notwithstanding an undiminished ingestion of food, because the power of absorption is restricted. Ordinarily the absorption of nutrient material from the intestine, in cases of diabetes, proceeds most satisfactorily,[17] so that the feces contain scarcely any more nitrogenous substances, fat and carbohydrates, than in health. But with the onset of diarrhœa the conditions are changed, absorption is checked, and this acts in the same way as a diminished ingestion of food.

But this does not exhaust the list of causes that go to lessen glycosuria in acute digestive disorders, for often this decrease is more pronounced than could be accounted for by a reduced ingestion and absorption of nutrient material. Experience has taught us to regard such an excessive diminution of the glycosuria as a *signum mali ominis*, for it is a symptom which may accompany or herald the dreaded diabetic coma. Of this we shall speak later.

Besides acute gastro-intestinal disturbances chronic affections of the digestive organs may also exercise an important and permanent influence upon the excretion of sugar in the urine. Although the process of absorption, as it goes on in the great majority of sufferers from diabetes, leaves little to be desired, there are still exceptions to this rule. In some of these cases the stools are of enormous size, of a thick pulpy consistence, dirty dark-gray in color, and greasy in appearance. Microscopical examination shows the presence of large fat globules, crystals of soap and fatty acids, and numerous muscular fibres. The results of chemical analysis accord with this microscopical picture. Hirschfeld, who has made a special study of these cases, recovered on an average 35.2 per cent. ash, 31.8 per cent. nitrogenous

substances, and 34.8 per cent. fat, which had been taken in by the mouth, in the feces; the normal figures are from 6 to 7 per cent.

All our experience hitherto indicates that, in these cases, we have to do with pancreatic diabetes, and that the changes in the pancreas must be of such a kind that not only the "internal secretion," which regulates sugar consumption (*cf.* p. 53), but also the discharge of the pancreatic juice into the intestine, is seriously interfered with. The facts gleaned from experiments upon animals speak with special force in support of this view, for identical anomalies of absorption are seen after extirpation of the pancreas in dogs (Minkowski, Abelmann, Sandmeyer). My experience has been that the glycosuria in these cases (which, it may be remarked, are very rare) is subject to greater and more sudden oscillations in intensity than it is in other forms of diabetes, notwithstanding an unchanged dietary. I have repeatedly examined the feces with a view of determining the cause of these sudden and pronounced oscillations, and have found that the condition of absorption is subject to corresponding change, being now better and now worse. The external appearance of the patient betrays none of these changes.

9. *Relation of Glycosuria to Intercurrent Diseases.*

I have already had occasion to note the fact that in many cases of diabetes the urine becomes less saccharine or entirely sugar-free during the intercurrence of an *acute pyretic infectious disease.* This is an old experience. Typhoid fever and relapsing fever are most commonly known as glycosuria-lessening; I have observed the same result in fibrinous pneumonia and influenza. Chronic diseases accompanied by fever, pulmonary tuberculosis in particular, have less influence in causing a diminution of the glycosuria.

We cannot always count with certainty upon the occurrence of this phenomenon, individual cases reacting in various ways. The symptom is of evil prognostic import, and as a general rule it may be said that the more marked it is the lower has the patient's strength been reduced by the intercurrent disease. Doubtless the loss of appetite and diminished ingestion of food, accompanying the acute disease, have something to do with this; but they do not explain all, for it may be observed that a diabetic, during an attack of pneumonia, will bear large quantities of farinaceous food which would inevitably induce marked glycosuria if eaten at any other times. It is possible that the ferments produced by the specific bacteria and circulating in the blood may give a fillip to the cells, enabling them to dispose more effectually of the sugar molecule for the time being. There is a field

here for further investigation, and it is possible that it may lead to discoveries of therapeutic value.

A reduced excretion of sugar accompanies the *final stages* of diabetes more often than it does the acute infectious diseases. It sometimes happens that a patient with diabetes is brought to the hospital in a state of coma; the urine contains no sugar; the patient dies, and the diagnosis of diabetes mellitus is made on pure conjecture; afterward it is learned from the statements of the relatives that the man had suffered from diabetes. Without doubt the condition of complete inanition in which a patient with diabetic coma exists for several days is the cause of the disappearance of the glycosuria. The abstinence from food brings with it a marked diminution in the decomposition of albumin and thus actively lessens the formation of sugar in the organism.

It is interesting and noteworthy that the glycosuria very often disappears in patients in whom—whether as a consequence or not of the diabetes—*granular atrophy of the kidney* has developed (Frerichs, Stocvis, Fürbringer[18]). The diabetes is cured, but we do not know the connection. The fact is, however, important, because the transition from diabetes to nephritis must be regarded as rather favorable than otherwise.

Finally it may be recalled that sufferers from diabetes, who are at the same time subjects of the *gouty diathesis*, as a rule pass urine that contains no sugar during an attack of the gout—diabetes alternans (*cf.* p. 68).

II. Effects of Glycosuria upon Nutrition and Metabolism.

(Emaciation, Polyphagia, Proteid Decomposition.)

Our present knowledge concerning the consumption of nutrient material and its relations to force and heat production in the body enables us to obtain a clear understanding of the consequences which glycosuria must bring with it as regards metabolic equilibrium.

1. *Calorie-change, General Nutrition.*[19]—It was formerly believed that the process of oxidation is lowered in the diabetic organism, that is to say, that the kilogram of protoplasm requires for the exertion of the same force less fuel, consumes less oxygen, and sets free less CO_2, than in health. This view was in notable conflict with the law of the conservation of force. The works of Carl von Voit, Leo, Weintraud, and Laves show that the diabetic converts just as much potential energy into living force as the healthy individual. Between the diabetic and the healthy individual at rest, and between the working diabetic and the working healthy man there is in this respect no difference.

Before entering upon a study of the special conditions obtaining in the diabetic, a few physiological considerations must be premised. Following the suggestion of Rubner it has become usual to measure the manifestation of force which reaches its development through oxidation processes in the body by the physical unit value of the calorie (heat-unit). By the word calorie is understood the amount of heat necessary to raise one kilogram of water 1° C. Careful investigations have shown that every one of our nutritive substances by its consumption in the body produces an exactly definite amount of heat or the mechanical equivalent of this measure in the form of energy.

1 gm. of albumin, by its conversion into urea, water, and carbonic acid, yields	4.1 calories	in heat or work.
1 gm. of carbohydrate, by its conversion into water and carbonic acid, yields	4.1 calories	
1 gm. of fat, by its conversion into water and carbonic acid, yields	9.3 calories	
1 gm. of alcohol, by its conversion into water and carbonic acid, yields	7.0 calories	

Further investigations have established the value as fuel of the materials daily consumed in the body. An adult man consumes in the twenty-four hours, per kilogram of body weight, material to the value of

30 to 35 calories, when at rest.
35 to 40 calories, when in motion and engaged in light work.
40 to 50 calories, when engaged in labor of moderate severity.

In order that the body may maintain its metabolic equilibrium the output must be met by an equivalent income of nutritive material, otherwise emaciation takes place.

An example will explain the position of the diabetic sufferer:

Mrs. B., 32 years of age, weighing 55 kilograms (121 pounds), occupied with light employment. Her nutritive needs were estimated at $55 \times 35 = 1{,}925$ calories. She took daily for five days:

Albumin	148 gm.	= 606.8 calories.
Fat	102 gm.	= 948.6 "
Carbohydrates	180 gm.	= 738.0 "
		2,293.4 "

She excreted a daily average of 141 gm. of sugar and lost in this way each day nutritive material to the value of $141 \times 4.1 = 578$ calories. The food taken had for her, therefore, the value of only $2{,}293 - 578 = 1{,}715$ calories. As we estimated the nutritive needs at 1,925 calories, there was a daily deficit of $1{,}925 - 1{,}715 = 210$ calories.

The body must, therefore, in order to meet the requirements of energy and heat production, have consumed of its own substance to the value of 210 calories. In this case we were able to determine what substances these were. The patient ingested each day 148 gm. albumin, containing 23.68 gm. nitrogen. In the urine there was found on an average 23.3 gm. nitrogen, and in the feces an average of 1.9 gm. nitrogen—a total of 25.2 gm. nitrogen. The patient consequently lost a daily amount of $25.2-23.68=1.52$ gm. nitrogen, corresponding to a loss each day of 9.5 gm. albumin. Through the decomposition of 9.5 gm. albumin are produced $9.5\times4.1=38.9$ calories. There remain, therefore, $210-38.9=171$ calories to be produced, which production must be obtained by the consumption of some non-nitrogenous substance. The only substance which enters into consideration is fat. In order to produce 171 calories 18.4 gm. of fat must be burned up ($18.4\times9.3=171$).

We see from this that a diet which would be a liberal allowance for a healthy person may be insufficient for one with diabetes. The diabetic must accordingly, in order not to waste away, either live on a mixed diet of higher calorie value than a healthy person, or else so compose a diet corresponding to his needs that a loss of sugar to any considerable degree may be prevented. He must from the nature of the case resort to albuminates and fat. An individual suffering from a severer grade of diabetes cannot be nourished by carbohydrates, for they would pass through him unconsumed like water through a sieve. (See the section on Treatment.)

We now understand the remarkable nutritive requirements, the polyphagia, of the diabetic. The sufferer from this disease, whose diet is not regulated by medical advice, swallows great quantities of food including much carbohydrate. The "stomach hunger" is momentarily stilled, but quickly returns, for the "tissue hunger" is not satisfied. The inordinate appetite of the diabetic disappears only when the useless carbohydrates are cut off and their place supplied by albumin and fat. When this is done the emaciation of the patient comes to a halt with the relief of the polyphagia.

2. *Proteid Decomposition.*[20]—The example just cited gives us an opportunity to discuss another point in the metabolism of the diabetic, namely, the albumin-change. It has for a long time been known that diabetic patients usually excrete a very considerable quantity of nitrogen (urea). Larger figures are not reached, indeed, in any other disease. Many authors, more particularly in France, have given a special name, azoturia, to this symptom. The azoturia is in great measure occasioned by the abundant ingestion of proteids. Diabetics often take, in the form of meat, eggs, ham, sausage, etc.,

from 180 to 200 gm. or more of albumin. The excretion in the urine of the nitrogen herein contained—except for the small amount passing away in the feces—is a physiological process. The healthy man, who ordinarily does not take in more than half this amount of albumin, excreting usually from 14 to 16 gm. of nitrogen, would excrete proportionately large amounts of nitrogen if his diet were increased to the same extent.

The condition becomes a pathological one only when the amount of nitrogen in the urine exceeds that taken in with the food, in other words when, in addition to the albumin of the food, that of the tissues also is decomposed. This occurs in diabetics when, as in the example above given, so much sugar is excreted that after the subtraction of its heat value from the heat value of the food the latter is found to be insufficient. Whenever an individual eats less than the necessities of his organism demand he loses in body substance, partly albumin and partly fat; in diabetics with little adipose tissue the loss of albumin is always proportionately the greater, its nitrogen being added to that of the albumin of the food. This waste of nitrogen is the greater the more the food value is depreciated by glycosuria. It is very large as long as the diabetic is left to himself to ingest the carbohydrates which are useless to him, but becomes slight or ceases when the diet consists largely of proteids and fat (Lusk, F. Voit, von Noorden, Hirschfeld, Weintraud).

The loss of nitrogen may also reach a high figure as a result of the action of toxic substances upon the protoplasm. Substances of this kind prejudicial to the integrity of the protoplasm are probably often formed in diabetes. I refer particularly to the final stage of the disease, diabetic coma. Nevertheless the existence of an azoturia of toxic causation in diabetes has never been determined with certainty.

III. Other Characteristics of Diabetic Urine.

1. *Quantity of the Urine; Specific Gravity.*—Polyuria is one of the most striking symptoms of diabetes. It often causes the patient uneasiness before any other phenomena of the disease are noticed. The desire to urinate often wakes the patient and forces him to get up, although as a general rule, if not always, the quantity of urine secreted during the night is less than that secreted during the daytime. This is worthy of note, since in other sufferers from a pathologically increased diuresis it frequently happens that from two-thirds to three-quarters of the entire amount of the urine is secreted during the night (Quincke).

The total volume of urine secreted in the twenty-four hours

amounts in many cases to 10 litres (17½ pints) or more—sometimes even 15 or 20 litres! In cases of moderate severity, where there has been no regulation of the diet, the average quantity secreted is from 4 to 6 litres (7 to 10½ pints).

An increase in the amount of sugar brings an increase in the amount of urine; but ordinarily the amount of urine rises less rapidly than does that of sugar, so that when the volume of water is greater the percentage of sugar is increased. The specific gravity is consequently higher the greater the amount of urine secreted—a phenomenon that is not observed in any other disease. The following tabular view, made up from a large number of urinary tables, shows the specific gravity and percentage of sugar corresponding to given amounts of daily excretion of urine. It must be remembered, however, that individual cases frequently present exceptions to the averages here given:

Total amount of urine expressed in litres.	Specific gravity.	Percentage of sugar.
1.5– 2.5	1.025–1.030	2–3
2.5– 4	1.030–1.036	3–5
4 – 6	1.032–1.040	4–7
6 –10	1.036–1.046	6–9

The relation of the amount of sugar excreted to the total volume of the urine is shown very clearly when the patient is transferred from a mixed diet to one consisting of meat and fat; the quantity of urine immediately falls and along with it that of the sugar, although never in exactly the same ratio. This is shown in the following table from E. Cless:

	Total amount of urine.	Specific Gravity.	Percentage of sugar.
Mixed diet (daily average of four days)	6,360 c.c.	1.038	7.05
Animal diet (daily average of seven days)	3,800 c.c.	1.031	2.2

If, under the influence of a strictly meat diet, the urine becomes entirely or nearly free from sugar, then its daily secretion approaches the normal amount. But the specific gravity remains higher, because the urine is rich in the end products of the meat ingested. There are many exceptions to the rules above given. Some may be formulated, others defy any schematic representation.

a. The glycosuria is often preceded for a rather long period by greatly increased diuresis; the urine in this case is of low specific gravity and resembles that in diabetes insipidus, but it is better to call it premonitory polyuria than diabetes insipidus, for in the present state of our knowledge everything points to the latter as being a disease *sui generis* and having nothing to do with diabetes mellitus. It is very interesting to note that many authors have observed only

polyuria after experimental injury to the pancreas, and not glycosuria; if diabetes mellitus did not ensue the polyuria rapidly disappeared.

b. When a cure of diabetes mellitus takes place, there often follows a period, extending over weeks or months, of polyuria without glycosuria. In many of these cases the explanation lies in the fact that the patients have acquired a habit of drinking large quantities of water which they cannot easily abandon. If the amount of water is lessened under the physician's orders, extreme thirst is felt for a number of days, but this gradually subsides and a normal diuresis is established. In other cases the thirst cannot be overcome, and the patients lose their appetite, sleep poorly, and feel depressed whenever the attempt is made to reduce the polyuria by restricting the allowance of water.

c. There are some rare cases of diabetes mellitus in which, despite a large percentage of sugar, only a normal quantity of urine is secreted, and the demand of the organism for water does not exceed physiological limits. The causes for this unusual condition are not known. Peter Frank first described these cases a hundred years ago, naming the condition "diabetes decipiens."

d. The natural ratio between diuresis and glycosuria may be disturbed artificially in various ways. A diminution in the amount of urine through reduction in the quantity of water can seldom be brought about, as experience has shown that diabetics bear this very poorly, and if it is insisted upon simply disobey. On the other hand the reverse often obtains. In patients undergoing a "drink cure" the urine is naturally largely diluted; it increases in amount while the specific gravity falls and the percentage of sugar is proportionately reduced.

2. *Consequences of the Polyuria.—a. Polydipsia.*—In diabetes mellitus, contrary to what obtains in many cases of diabetes insipidus, the polyuria is always the primary, and the exaggerated thirst (polydipsia) the secondary, condition. The thirst is great and calls aloud for satisfaction, yet it is seldom so extreme as in diabetes insipidus.

b. Fluidity of the Blood.—The kidneys irritated by the sugar draw such a volume of water from the blood that a certain amount of thickening of the latter may result. In such cases the proportion of solid constituents is increased, and examination shows a larger amount of hæmoglobin and red blood corpuscles than normal. But this apparent increase of the solid matter of the blood is always slight and is not constant, and there may be cases in which the fluid portion is normal or even relatively increased. We are still unable to formulate any definite law in this respect, notwithstanding the many data in our

possession. It is possible that many interesting relations may be brought to light when, in addition to the examination of the blood, the amount of fluid ingested and the sensible and insensible losses of water from the organism are also taken into account.

c. Transpiration of Water through the Skin.—Diabetics usually have a dry skin and can with difficulty be made to perspire. The reciprocal relations of the skin and kidneys being known, it is very easy to see that the increased activity of the latter is responsible for the inactivity of the former. There are exceptions, however, to this rule, but these relate only to mild cases of diabetes and usually to those occurring in corpulent individuals. Instances of unilateral or local sweating are to be regarded from a very different standpoint; these are to be explained by a pathological irritation of the specific nerves regulating the cutaneous secretion. The insensible perspiration is also diminished. Owing to the enormous drain through the kidneys, a relatively small amount of water is present to be disposed of by evaporation, but the absolute amount of water evaporated from the skin also is often lessened. That an absorption of water through the skin (negative insensible perspiration) takes place was formerly asserted but has not yet been determined with certainty.

3. *Nitrogenous Constituents of the Urine.*—We need add but little concerning the amount of nitrogen excreted; that is dependent upon proteid decomposition, and has been already referred to on page 88.

a. Urea.—This is true especially of urea, which is responsible for about 80 or 90 per cent. of the nitrogen in the urine and therefore is subject to the same laws that regulate the excretion of nitrogen in general. Of much greater interest is the excretion of

b. Ammonia.[22]—The healthy man excretes from 0.5 to 1 gm. of ammonia per diem, and this amount may rise to from 1.2 to 1.5 gm. when meat constitutes a large part of the diet. In many cases of diabetes the same proportion holds, but in other cases the quantity of ammonia may be much greater. An excretion of from 3 to 6 gm. a day has been frequently observed (Hallervorden, Stadelmann, Minkowski, Wolpe, von Noorden, and others), and Stadelmann even found as much as 12 gm. a day in one instance. The highest figures belong almost exclusively to the stage of diabetic coma; those between the extremes, on the other hand, may be observed in given cases for periods of weeks and months.

So far as we know the animal organism excretes increased amounts of ammonia when acids, which combine with ammonia and prevent its union with carbonic dioxide to form urea, have obtained entrance into the blood (Schmiedeberg, Stadelmann, Minkowski, and others). This rule appears to hold good with special force in diabetes, for

(1) The nourishment of diabetics is an "acid" one. Much phosphoric acid is formed from the large quantity of meat, etc., ingested, and in particular a large amount of sulphuric acid is produced by the oxidation of the sulphur which every albumin molecule contains.

(2) Besides this large quantities of organic acids are formed under certain circumstances in the diabetic organism. Aceto-acetic and beta-oxybutyric acids are much the most frequently produced of these organic acids. The conditions of their formation will be treated of later. With the exception of a few, as yet unexplained, cases (Wolpe), the presence of these acids in the urine is always accompanied by a profuse excretion of ammonia.

c. Creatinin often appears in diabetic urine in quantities that could hardly be reached in health—1.5 to 2 gm. per diem. The cause of this profuse excretion is to be found in the nature of the diet, for whoever eats a large amount of creatinin-containing meat must excrete correspondingly large quantities of this substance. A second source of creatinin is present when the patient, as so often happens in diabetes, consumes his own muscular tissue (*cf.* p. 89).

d. Uric Acid.—When proper methods of research are employed, normal or only slightly increased amounts of uric acid are found in the urine (Startz[23]). Contrary results are due to the employment of faulty methods. According to some French authors, there are cases of diabetes which are accompanied by an increased excretion of uric acid, and other cases in which uricaciduria and glycosuria alternate. These cases are referred by the writers who report them to "diabetes alternans."

e. Albumin.[24]—Statements concerning the frequency of albuminuria in diabetes vary greatly, the numerous statistics given making the percentage all the way from 10 to 68.7 (Bouchard, Fürbringer, Schmitz, Salles, Bussière). The albuminuria is almost always slight. Pathological anatomy teaches us that sufferers from diabetes seldom have perfectly healthy kidneys. Perhaps the organ becomes diseased in consequence of the enormous tax put upon it by the excretion of such large quantities of water, nitrogenous substances, and sugar. Others believe that the kidneys are poisoned by the definite products of metabolism in the diabetic organism. Albertoni, Trambusti, and Nesti inculpate the aceto-acetic acid. Nothing definite, however, is known on this point. Concerning the transition of diabetes into granular contracted kidney, see p. 86.

4. *Non-Nitrogenous Organic Substances.—a.* Acetone, aceto-acetic acid, and beta-oxybutyric acid are the most frequently encountered of these substances. All these bodies, especially the first two, have been made the subjects of numerous publications; the literature in-

deed is so voluminous as hardly to be gone through with. I have myself made an exhaustive study of these bodies, not only in diabetes but in other diseases as well, and I must, in order not to draw the discussion out to too great lengths, confine myself in general to the expression of my own views. The common source of acetone, aceto-acetic acid, and oxybutyric acid is without doubt albumin. During the normal decomposition of albumin in health at most only traces of acetone (about one centigram) are excreted. In cases in which the amount of acetone is increased and the other substances appear in the urine, either

(1) There is a splitting up of the albumin molecule as regards its non-nitrogenous derivatives, which normally does not take place, or

(2) The normal decomposition proceeds as far as the formation of the above-mentioned substances, and then ceases, or finally

(3) These substances are formed through the decomposition of certain kinds of albumin only, while they are absent in the decomposition of the ordinary albumin of the food.

We cannot answer these questions definitely until the still disputed point as to whether acetone and the other bodies are normal intermediate products of the retrogressive metamorphosis of albumin, is settled.

Acetone and *aceto-acetic acid* have so many points in common that they doubtless owe their origin to one and the same process affecting the albumin molecule, and indeed it appears probable that aceto-acetic acid is the mother-substance of acetone. When but little aceto-acetic acid is formed the entire amount becomes converted into acetone, but when a large amount is formed a part of it appears in the urine together with the acetone. The conversion of the acid into acetone possibly takes place in the urine, but in addition to this it certainly occurs within the tissues or in the blood, as the volatile acetone is found in the expired air. Since aceto-acetic acid, even outside of the body, is transformed with extreme facility into acetone, there is nothing against the probability of this assumption.

I called attention two years ago to the fact that always, whenever large quantities of acetone and aceto-acetic acid appear in the urine, the albumin of the body is being destroyed—in consequence either of insufficient nourishment, starvation, or of a poisoning of the protoplasm by enterogenous toxines and bacterial products. I have concluded from that that the formation of these substances takes place only during the decomposition of the albumin of the body, and never during that of the albumin of the food.

The facts of diabetic acetonuria and diaceturia can be brought into

agreement with this conclusion, for we have seen that the diabetic is often in the condition of consuming his own proteids. In fact I have myself seen a high degree of acetonuria and diaceturia in diabetics only when the output of nitrogen was greater than the income. Furthermore, whenever cases are reported in the literature, as they frequently are, in which acetone is excreted in the urine to the amount of several decigrams or grams (even as much as 10 grams) a day, we are always able to see, from the facts given in relation to the diet and to the glycosuria, that there must have been quite a considerable waste of the albumin of the body.

Beta-oxybutyric acid is perhaps, as many believe, the first stage in the formation of aceto-acetic acid. Clinically, however, it presents a certain independence, and I regard it as more probable that oxybutyric acid on the one hand and aceto-acetic acid on the other arise from qualitatively different decomposition processes.

Similar relations to those existing between the decomposition of albumin and the formation of acetone are not observed in regard to oxybutyric acid. The latter is regularly absent in diabetics who are in good physical condition, and not infrequently also in those who are suffering from a marked loss of body albumin. While oxybutyric acid is permanently absent in a certain number of cases of diabetes, and is not necessarily present even in those who are greatly reduced by pulmonary tuberculosis and other complicating diseases, other diabetics begin after a certain time, and without any cause that we can detect, to excrete it. Sometimes the daily amount excreted is only a few grams, at other times it reaches 50, 100, or 150 grams. After the excretion has once begun, it is never interrupted for more than a few days at a time; it is permanent and shows a constant tendency to increase. According to all our experience up to the present time, the symptom is of the gravest prognostic significance; in most cases, at the end of a few days or weeks, diabetic coma ensues and the case passes on to a fatal termination.

b. Relation of these Substances to Diabetic Coma.—Upon the ground of the just-mentioned temporal coincidence, many authors look upon diabetic coma as an "acid intoxication" (Stadelmann, Minkowski, von Jaksch); others regard it as the result of a specific poisonous action of oxybutyric acid or the substances allied to it; while others again would attribute to acetone and aceto-acetic acid as well an important rôle in the etiology of diabetic coma. The last-named opinion is hardly tenable. I have often, as have also other observers, seen marked acetonuria and diaceturia continue in diabetics for weeks or months at a time and then disappear again. During this period the patients grew weaker and lost in weight in conse-

quence of the profuse acetonuria, but they presented no symptoms of coma. These observations prove more than do those in which stress is laid upon the consecutive relation of acetonuria and coma. Acetonuria and diaceturia are found so frequently and indeed so regularly in weakened diabetics with well-marked paralysis of the sugar-consuming functions and in those in whom there is an increasing difficulty in obtaining sufficient nourishment, that we need not wonder at their presence among the conditions preceding coma. But it is not permissible to predicate an etiological from a merely temporal relation.

Much more difficult is the question of oxybutyric acid, the appearance of which in diabetes is always followed in time by coma, unless death is occasioned by some intercurrent disease. The views held concerning this substance are flatly contradictory. I incline to the opinion of Klemperer, according to which, in some stages of diabetes, for reasons unknown to us, certain toxic substances are formed. These poisons act (1), after a certain accumulation has taken place, as paralyzants of the brain, inducing coma, and (2) as destroyers of protoplasm. When large quantities of oxybutyric acid are present in these cases we must attribute to the active poison in diabetes the special property of conducting the decomposition of albumin along the special lines leading to the production of this acid, for in other forms of destruction of protoplasm (starvation or fever) there may be occasionally an excretion of oxybutyric acid in the urine, but it is always in the most minute quantities. Coma on the one hand, and the formation of oxybutyric acid and reduction of the alkalinity of the blood on the other, would be, according to this, not subordinate but co-ordinate phenomena.

Theory apart, it may be asserted that acetonuria and diaceturia appear whenever for any reason a diabetic is unable to take as much nourishment as his needs demand. They are important as an admonition to attend carefully to the regulation of the diet, for any lowering of the nutritive conditions may hasten the occurrence of coma or in some other way lead to a fatal termination. The excretion of oxybutyric acid is of the gravest prognostic import unless it ceases again in a few days, for it renders the speedy onset of coma very probable.

5. *Mineral Constituents of the Urine.*—Chloride of sodium and sulphuric and phosphoric acids are found usually in the urine of diabetics in greater quantities than in that of healthy persons. That is readily explained by the greater quantity of food ingested by diabetics. As regards sulphuric and phosphoric acids especially, the great consumption of flesh meats, and also, when present, the pathological de-

composition of proteids, are significant. The daily excretion of five or six grams of each of these two acids is not uncommon. In general the parallelism between them and the urea is maintained. According to the investigations of van Ackeren, of Chicago, diabetics often excrete such large quantities of phosphoric acid and lime, as compared with the proportions of these substances contained in the food, that we have to assume a waste of some tissue of which they form an important constituent; such tissue can only be the osseous.

6. *Pneumaturia.*[253]—In certain rare case of diabetes air is voided with the urine, passing out from the urethra with a peculiar bubbling noise. This pneumaturia has been observed in both men and women. It may of course be caused by the entrance of atmospheric air or of intestinal gases into the bladder, when any lesion (ulceration, etc.) of these parts has led to the formation of a fistula. Such cases differ in no way from similar ones occurring in non-diabetic individuals.

The peculiar form of pneumaturia which has been observed especially in diabetes arises from a formation of gas in the bladder itself in consequence of decomposition or fermentation processes in the urine. The subject of the fermentation is the sugar, the excitants of the fermentation are micro-organisms which in some way, through the passage of a catheter or the occurrence of cystitis, have obtained entrance into the bladder. In the reported cases the micro-organisms were not always the same, among those noted being the bacillus of butyric acid fermentation, the bacterium coli commune, the yeast fungus, and other sorts. The gaseous products of the fermentation are carbon dioxide (CO_2), hydrogen (H_2), and methane (CH_4); other products of the fermentation of carbohydrates found in urine of this sort are butyric acid and lactic acid. Besides the micro-organisms which seize upon the carbohydrates, other microbes which act upon the albuminoids may occasionally gain entrance to the bladder and, when albumin is present, give rise to the formation of sulphuretted hydrogen gas (SH_2). This form of pneumaturia (hydrothionuria) may of course occur in other individuals as well as in diabetics.

The pneumaturia of diabetes is always a very troublesome complication and one difficult of remedy. Almost inevitably cystitis develops if this have not already existed and contributed to the production of the pneumaturia. Persistent local treatment, consisting in repeated washing out of the bladder with antiseptic solutions, is often necessary in order to restore the bladder to an aseptic condition.

IV. Chemistry of the Other Secretions.

1. *Saliva.*[26] Amount.—The mouth of the diabetic, despite the large and frequent draughts of water, shows an obstinate tendency to become dry. The saliva is as a rule scanty and poor in ferment, although there are exceptions. In many patients the secretion is normal and in others there may even be a very amazing degree of ptyalism. In some cases I have failed to obtain the sulphocyanic reaction in diabetic saliva.

Sugar.—The accounts given of the presence of grape sugar in the saliva are very unreliable. If this substance is ever found it is only exceptionally.

Reaction.—The mixed buccal secretions are as a rule of acid reaction in diabetes. According to the results of Mosler's and von Frerichs' researches it appears to be certain that even the parotid secretion as it flows from Steno's duct may be faintly acid. This happens occasionally also in healthy individuals, but then only temporarily (Sticker).

2. *Gastric Juice.*[27]—The secretion of hydrochloric acid has been examined by Honigmann, Rosenstein, and Gans in twenty-eight cases of diabetes, but no law concerning it could be discovered. These authors found the secretion usually below the normal amount, in some cases variable. A diminution, if it occurs, is to be referred, according to Rosenstein, to nervous influences.

3. *Intestinal Secretions.*—Since it is impossible to collect the intestinal juice in a pure state, its secretion must be estimated from an examination of the feces. It has been already stated that the feces in diabetes are as a rule normal in amount and composition, and that the absorption of nutritive material proceeds satisfactorily (*cf.* p. 84). It was also at the same time pointed out that occasionally exceptions may be met with which are to be attributed to a deficient access of the pancreatic juice.

4. *Semen.*—Diabetics often have increased sexual desires at the beginning of the disease, but this stage is usually of short duration and the opposite condition soon prevails. Patients frequently complain, even in the early stages of the disease, of a loss of virile power and of a reduced seminal secretion, and these phenomena are to be counted among the regular symptoms of the later stages, if we except the mildest cases. But there are occasional exceptions to this rule. Frequently the impotence is the first symptom that leads the patient to seek medical advice.

5. *Perspiration.*—The condition of the cutaneous secretion has already been referred to on page 92. The earlier reports concerning

the appearance of sugar in the sweat in diabetes were, to say the least, exaggerated (Külz), for the occurrence is in any case extremely rare. I have examined the sweat, after injections of pilocarpine, in six cases of diabetes, and never found any substance in which fermentation could be excited by yeast or which formed the characteristic crystals upon the addition of phenylhydrazin.

V. Chemistry of the Blood.

1. *Sugar.*—That the percentage of sugar in the blood is greater than normal in every case of diabetes in which glycosuria is present has been already stated a number of times in this treatise. The glycosuria is the consequence of the hyperglycæmia. In contrast to the normal amount of from 0.5 to 1.5 per mille, Pavy among others reports from 1.54 to 5.76 per mille, Seegen, in grave cases, from 2.3 to 4.8 per mille. The proportion is not always constant in each case, but varies, contrary to what obtains in the healthy organism, according to the nature of the food; the ingestion of carbohydrates increases it, the withdrawal of these substances diminishes it. In general there is an exact relation between the amount of sugar excreted in the urine and that contained in the blood.

There is still much that is obscure in this field; further research into the reciprocal relations of diet, blood-sugar and urine-sugar is urgently needed and promises good results as regards our knowledge of diabetes. In the mean while these investigations are difficult of execution and uncertain in their results, for the reason that we possess no exact method by which we can estimate correctly the presence of small amounts of sugar in the blood.

2. *Glycolitic Ferment.* See page 54.

3. *Water and Permanent Constituents.* See page 91.

4. *Fat.*—In grave cases fat has quite often been found in the blood in such quantity that the serum was milky. I have convinced myself that this lipæmia was not connected with a previous ingestion of fat. What is the cause and what the result of this transportation of fat in the blood, and in general what the significance of the phenomenon may be, are unknown. If the lipæmia becomes excessive it may result in lipuria, that is, in the passage of an extremely fine fat emulsion through the kidneys.

5. *Alkalinity.*—In patients who enjoy excellent general health the alkalinity of the blood is normal, but in those who are very much reduced in strength it is always diminished. The alkalinity has been found to be less than in any other disease in diabetics who had reached the stages of oxybutyric acid excretion, or who were already

comatose. The alkaline value of the blood in such cases has been found to be only 40 milligrams of sodium hydrate (NaHO) per 100 grams of blood; the normal value is 350 to 400 milligrams. As has been shown above, the alkalinity of the blood is lowered by the production of abnormal acids. For a discussion of this point and of the relation of a diminished alkalinity to coma, see page 95.

I would say here that I have come to regard with great distrust the methods hitherto employed for determining the degree of alkalinity of the blood, and this on the ground of certain investigations which Löwy has most carefully carried out, at my suggestion, upon patients in the Charité Hospital in Berlin. Perhaps the near future will see a fundamental change in our views on this matter.

COMPLICATIONS OF DIABETES.

I. Frequency and Causes of the Complications.

Diabetes is a disease that shows an extraordinary tendency to complications; almost every organ of the sufferer from this disease may become the seat of some pathological process. The disturbances met with differ for the most part but little or not at all from those encountered in previously healthy individuals or in persons who have been suffering from some other disease. Certain of the pathological processes, however, receive a special impress under the influence of the diabetes, so that, partly from certain special characteristics, partly from their course, and partly from the peculiar grouping together of the organic diseases, it may be possible to arrive at a diagnosis of diabetes mellitus as the primary disease even before the examination for sugar in the urine has given the final proof of its existence.

There has been much discussion as to the causes of the manifold organic affections occurring early or late in the course of diabetes. The complications have at times the character of an inflammation, at times that of simple disturbance of nutrition, of necrosis, or of degeneration. Some writers inculpate chiefly the bad general nutritive condition which reduces the powers of resistance of every portion of the body and favors the action of new injurious influences not connected immediately with diabetes. Among such influences are to be reckoned traumatism and over-strain as well as infections.

Other authors believe that the high percentage of sugar in the circulating fluids exerts a direct injurious influence upon the organs, whether by withdrawing water from the tissues or by impregnating them with a concentrated saccharine solution; the sugar acts as a

poison to the tissues. I may mention as a representative of this doctrine Naunyn, who gives the following list of symptoms and diseases as caused by the high percentage of sugar in the fluids: Neuralgia, neuralgic pains, angina cordis, asthma, pruritus, eczema, impotence, inflammations with a tendency to gangrene, scorbutus, boils, carbuncles, cataract, morbid hunger and thirst. The high percentage of sugar in the fluids is regarded as injurious from another point of view also. Grape sugar, as is well known, favors the growth of a vast number of micro-organisms; the tendency of the diabetic to certain infectious diseases, especially tuberculosis, might therefore be due to the presence of a very favorable saccharine soil in the diabetic organism. Leo has approached this question experimentally by testing the resistance of healthy animals and of those made diabetic artificially to various pathogenic bacteria; he arrived, however, at no definite results. Unfortunately he used phloridzin to produce diabetes in his animals, overlooking the fact that there is no surcharge of the fluids with sugar in phloridzin diabetes (*cf.* p. 50).

A third view as to the etiology of the complications of diabetes is that, in addition to the undoubted evil results of the lowered nutritive conditions, there are certain toxic substances present which are prejudicial to the integrity of the organs. Their action is alleged especially in cases of degeneration and of functional disturbances. We do not know of any such poisons, it is true; but we can readily conceive that certain intermediary products may be formed during the morbid metabolism of the cells in diabetes which are poisonous and which find vulnerable spots in one or another organ. Such an explanation is more especially probable in respect to the nervous system, the great susceptibility of which to the action of mere traces of poison is made clear to us by the teachings of toxicology and pharmacology as well as by a study of the infectious diseases. I may instance the paralysis following diphtheria.

We are not yet so far advanced as to be able to discover the causes for all the complications of diabetes. Probably they are manifold. Practically the physician will do best who keeps always in mind the fact that every diabetic has less power of resistance against noxious influences than the healthy individual. It seems to me also to be of practical worth not to lay too great stress upon the presence of sugar in the blood as the injurious factor. Whoever regards this as the prime factor will too readily come to believe that he has done all that is necessary when he has prescribed a diet designed to effect the cure or improvement of the glycosuria, and that the great and pressing danger of complications is thereby removed. Such a belief on the part of the physician is distinctly false and prejudicial to the patient.

We now pass to a consideration of the individual complications of diabetes. In this section it will be sufficient in many places, in order to avoid needless repetition, to refer the reader to what has been discussed above.

II. Cutaneous Complications.

1. *Pruritus* is encountered in diabetes under many forms:

a. Generalized Pruritus.—This form is found especially in diabetics with marked polyuria and glycosuria, rapid emaciation, and great dryness of the skin. It may be presumed that the dryness of the epidermis irritates the cutaneous nerves passing between the epithelial cells. Many sufferers from diabetes present generalized pruritus as one of the earliest noticed symptoms of the disease. The phenomenon gradually disappears when the patients are put upon a diet which causes a diminution in the polyuria and glycosuria and with that a lessening of the dryness of the skin.

Besides the view here stated concerning the origin of the pruritus we may mention the theory that the cutaneous nerves are irritated by the sugar circulating in the fluids, and another that there is a central irritation reflected toward the periphery.

b. Pruritus of the Genitalia.—This form is much more common in women than in men, and is not seldom the earliest subject of complaint by diabetic women. The itching is at first localized on the inner and outer surfaces of the labia majora, extending thence to the neighboring parts (folds of the groin and inner surfaces of the thighs). All the parts indeed which are liable to be wetted by the saccharine urin may become the seat of this pruritus. The itching is, as has now been clearly shown, always caused by a growth of hyphomycetes which partly grow in the form of minute white collections upon the surface of the skin and partly, like the oidium albicans in the mouth, press in between the epithelial cells. Evidently the skin moistened with the saccharine solution offers a most favorable soil for the growth of this fungus (leptothrix and other similar varieties).

Occasionally, perhaps as a result of the fungous growth alone but most frequently and especially in consequence of the irritation from scratching, an inflammation arises which sometimes runs its course as a superficial dermatitis, at other times—when the microbes of suppuration have entered the cracks in the skin—may result in the production of boils and phlegmons.

Pruritus vulvæ and its consequences are naturally less frequently encountered in cleanly women than in those who are not. An English physician recently assured me that he had never observed the

symptom among his private patients, but had frequently seen it in hospital practice.

A similar condition is observed in man, but much less frequently; it is manifested by itching of the glans penis and prepuce, the formation of superficial colonies of the fungus, balanitis, and phimosis. The itching is felt especially at the meatus and may give rise to tenesmus. In other cases the scrotum is the chief seat of the pruritus.

2. *Inflammations of the Skin.*—The entrance and growth of microorganisms is a necessary condition for the production of furuncles. I have seen pure cultures of the staphylococcus aureus in three cases of furunculosis (ten boils in all). Furunculosis occurs in mild as well as in severe cases of diabetes, in the early and late stages, when the patient is on an animal diet as well as when he is indulging freely in carbohydrates—on an average in from one-tenth to one-fourth of the cases.

Subcutaneous phlegmons and carbuncles are not so common as boils. They always have their origin in cracks of the skin. The tendency to the gangrenous forms of inflammation, which is so pronounced in diabetes, is clearly shown in these cases.

While the point of entrance of the infecting germ is usually very readily found in cases of carbuncle and phlegmon, this is not the case with boils. They often appear when the skin is apparently unbroken. It was formerly regarded as certain that furuncles were due to an internal cause, being dependent upon a high percentage of sugar in the blood or else of trophoneurotic origin. The only thing that we can and must admit in this regard to-day is that the skin in diabetes opposes a less firm resistance to the entrance of microbes, and that for this reason a boil is produced where in healthy persons a small acne papule or only a little hyperæmia at the mouth of a follicle would be observed. Doubtless it often happens that pruritus first appears; the itching part is scratched, little cracks open in the epithelium, and through these, either from the scratching finger or from dirty underclothing, microbes enter the skin.

It follows from this that furunculosis is a complication of diabetes which can be prevented by careful attention to the skin, and it would appear that it has become more rare during the last few decades, in which a regard for personal cleanliness has become more universal among civilized people.

3. *Traumata.*—Wounds of the skin and also deeper wounds heal more slowly in diabetics; septic germs enter more readily, and granulation tissue has a tendency to slough. Although the healing of wounds in diabetics is much better now than it formely was, owing to the application of the principles of antisepsis and asepsis, yet fatal

delay in healing and spreading gangrene are still common enough. For this reason surgeons shrink, and justly, from the performance of any avoidable operation in cases of diabetes. Some operations have a particularly bad reputation, especially that for the relief of phimosis.

4. *Insensible Perspiration.*—See the section on the cutaneous secretion on page 92.

5. *Chemistry of the Sweat.*—See page 98.

III. Changes in the Mouth and Throat.

1. *Aphthæ.*—Little whitish patches are often seen on the gums of diabetic patients; they are slightly resistant when brushed away, and after their removal the spot where they were appears a little hyperæmic. These are colonies of oidium albicans, which finds a favorable soil in the loose epithelium sodden with a saccharine solution. The weakly acid reaction of the buccal fluids, which is the rule almost without exception in cases of diabetes, may also favor the growth of the fungus. Cases have occasionally been observed in which the aphthous organism has penetrated into the vessels of the mucous membrane and thence has been carried to the lungs and brain, giving rise to embolism in these organs. Aphthous stomatitis, like the fungous growth on the genitalia, belongs to the complications of diabetes which may be prevented by cleanliness.

2. *Gums and Teeth.*—Affections of these parts are exceedingly common, and very few diabetics escape them entirely. Gingivitis is frequent, as is also alveolar periostitis; the teeth become loose and readily fall out. This trouble often appears early, causing considerable annoyance, and not infrequently suggests to the dentist the advisability of examining the urine for sugar, so leading to the diagnosis of diabetes.

In other cases caries of the teeth is a more prominent symptom than the inflammation of the surrounding parts.

Evidently the cause of these troubles of the teeth and gums is to be referred to the lowered power of resistance of the tissues to attack by the schizomycetes, which are always so abundantly present in the mouth and take advantage of every injury of the gum and of every loosening of the dental periosteum to invade the parts. The simple loosening and dropping out of the teeth appears, on the other hand, to be due to the action of trophoneurotic causes.

The inflammatory and carious processes may doubtless be in great part, if not wholly, avoided by careful cleansing of the mouth. The use of too stiff tooth brushes is inadvisable, as they are likely

to produce slight wounds of the gums. The teeth should be brushed and the mouth rinsed out several times a day; the most suitable mouth-wash is a three-per-cent. solution of borax.

3. *Chemistry of the Saliva.*—See page 98.

IV. Changes in the Stomach.

1. *Gastroectasia.*—Dilatation of the stomach is not infrequently seen in diabetics, especially in those who have remained a long time without treatment and in order to cover the unrecognized loss of sugar have taken enormous quantities of food (*cf.* p. 88). There is usually a simple enlargement, the evacuation of the stomach not being delayed or interfered with (megalogastria), but sometimes there occurs a weakening of the muscular coat, leading to motor insufficiency and long-continued stagnation of the contents of the viscus. This is always a matter of grave import in diabetes, for the nutrition of the patient is now interfered with from two directions, firstly by the waste of valuable material through the urine, and secondly through the difficulty of supplying sufficient nourishment, which is associated with gastric disorders of whatever sort. In addition to simple stretching of the walls, there may also be a catarrh of the stomach or, seldom, gastric ulcer.

2. *Boulimia and Polyphagia.*—See page 88.

3. *Chemistry of the Gastric Juice.*—See page 98.

V. Changes in the Intestine.

1. *Defecation.*—In most cases of diabetes the bowels are regular, or at most there is a slight tendency to constipation. A loose action of the bowels is not common, although it may be observed. Some patients have one or two thin pasty evacuations daily, and feel very well in consequence.

2. *Intestinal Catarrh and its Relation to Coma.*—The case is very different when frequent attacks of diarrhœa occur in consequence of acute intestinal catarrh. Every acute catarrh of the intestine is a matter of serious moment for the diabetic. In the first place it interferes with the nourishment, forbidding especially the ingestion of any large quantity of fat, and secondly, experience has shown that diabetic coma is a frequent sequel of acute catarrhal enteritis. The views as to the relation which these two conditions bear to each other are various. Authors differ as to whether (*a*) the diarrhœa is simply the first symptom, a precursor, of the threatening coma, or (*b*) the toxic substances formed in the intestinal canal during a catarrhal attack are

absorbed and induce coma, or finally (*c*) the coma is merely a result of the general depression and interference with nutrition associated with catarrhal enteritis. I myself incline to the last-mentioned theory. But whatever the relation may be, diarrhœa is by no means a necessary accompaniment of diabetic coma, for it is absent in at least fifty per cent. of the cases.

On the other hand we must regard obstinate and long-continued constipation with suspicion. Schmitz in particular has drawn attention to the fact that coma is a frequent sequel to this condition. He believes that dangerous poisons may be resorbed from the stagnating contents of the bowel, and utters an urgent warning against allowing the bowels to remain constipated in cases of diabetes.

3. *Steatorrhœa (Fatty Stools).*—Whenever in cases of diabetes the feces contain much fat, as may happen in disorders of the pancreatic secretion and in stoppage of the biliary passages, the stools become very frequent, are pulpy, of a dirty gray color, and of putrid odor (*cf.* p. 84).

4. *Anatomical changes in the intestinal walls* are very seldom met with. In a few cases here and there catarrhal lesions of the mucous coat and brown atrophy of the muscularis have been observed.

VI. Changes in the Pancreas.[29]

Concerning the etiological significance of pancreatic changes enough has been said above (*cf.* pp. 51 and 71). We have here to see whether pancreatic diabetes betrays itself by any special signs and can be diagnosed. Not much use can be made at the bedside of such general data as Lancereaux has given, viz., specially malignant course, rapid emaciation, and tendency to pulmonary tuberculosis. This complex of symptoms is often enough observed in cases in which the pancreas is found healthy post mortem, or shows only such a reduction in size and softness in texture as could be easily accounted for by the generally lowered state of nutrition. Of more importance are the following symptoms: (*a*) Existence of a tumor of the pancreas (carcinoma, cysts, echinococcus); (*b*) severe colic which cannot be referred to the kidneys or the liver, but which by its location raises a suspicion of a calculus in the duct of Wirsung (Fleiner, Lichtheim, Holzmann); (*c*) excretion of maltose in the urine. This symptom has up to the present time been observed only twice (le Nobel, van Ackeren), and its significance is not yet clear; (*d*) steatorrhœa without jaundice; (*e*) azotorrhœa, that is to say, the passage of large quantities of nitrogenous substances in the feces. This symptom was noted in the cases of Hirschfeld referred to on page 84, as also in

experimental extirpation of the pancreas in animals (Minkowski, Abelmann, Sandmeyer).

These symptoms are individually seldom seen in diabetes, and all of them together are still more rarely encountered. The occurrence of the symptoms and a diagnosis of the condition presuppose not only that the internal secretion of the pancreas is interfered with, but also that there are at the same time certain gross anatomical changes present.

As regards the character of the lesions of the pancreas which have been noted, they were most frequently chronic interstitial inflammation (sclerosis), atrophy, fatty degeneration and necrosis of the cells; more rarely cysts, calculi, carcinoma, and echinococcus of the pancreas have been observed.

VII. Changes in the Liver.

1. *Disturbance of the Glycogenic Function.*—See page 57.

2. *The Bile.*[30]—The elaboration of the bile is not interfered with, so far as we know, in or by diabetes. On the other hand, we very frequently meet with gall-stones in diabetics, especially in corpulent patients. Bouchard found gall-stones in ten per cent. of his cases. Naunyn denies justly that there is any intrinsic relation between the two affections.

3. *Hepatic Diseases.*—It is unquestionable that we are often able to make out a moderate enlargement of the liver in many corpulent subjects of diabetes, and there is also a slight tenderness on pressure over the organ in these cases. In these instances there is almost always, besides the fatty infiltration, some venous hyperæmia which rapidly subsides under appropriate treatment. The hyperæmia is doubtless due more to the disturbances of circulation caused by the obesity than to any influence of the diabetes.

Other diseases, such as atrophic cirrhosis, hypertrophic cirrhosis, abscess of the liver, or carcinoma are met with as accidental complications. As to the considerations which may arise in case of a possible syphilitic affection of the liver see p. 72.

VIII. Changes in the Lungs.

1. *Tuberculosis.*[31]—Pulmonary tuberculosis plays a most important rôle among the complications of diabetes. It is not too much to say that at least one-fourth of all diabetic subjects among us in Germany contract pulmonary tuberculosis, and once they have contracted it, speedily succumb. Yet the distribution of the disease among different cases of diabetes is very unequal. When diabetes attacks youth-

ful subjects it is the rule that they become tuberculous, unless coma or some accidental intercurrent disease carries them off earlier. Older persons, especially the corpulent or gouty subjects, are in much less danger of this complication. According to Lancereaux, as has already been remarked (*cf.* p. 71), sufferers from pancreatic diabetes show a special tendency to tuberculosis.

It is a fact of common observation that tuberculosis attacks sufferers from diabetes among the poorer classes much more frequently than it does those in better circumstances. The former are naturally more exposed to infection by reason of their unfavorable hygienic surroundings and through their stay in hospitals which are always crowded with tuberculous patients. Because of this fact, physicians who have to treat chiefly well-to-do patients at watering-places (Seegen at Carlsbad, Durand-Fardel at Vichy) have sometimes come to the incorrect conclusion that tuberculosis is a rare complication of diabetes.

Tuberculosis may occur at any time in the course of the disease. Even the mildest forms of diabetes appear to increase the natural predisposition in man to tuberculosis. It may be asserted, indeed, that tuberculosis is an even more frequent complication of diabetes than appears from the statistics, for in many cases of pulmonary phthisis the urine is not examined for sugar and thus the diabetes escapes detection.

In addition to the rapidity of its course, pulmonary tuberculosis complicating diabetes presents other peculiarities. Hæmoptysis is, according to Leyden and Seegen, and also in my own experience, of very rare occurrence. Several authors have remarked that tubercle bacilli are found in small number or not at all in the sputum. I can recall a case occurring in my own practice of a patient whose lungs were very extensively diseased and whose sputum consisted of the usual tenacious, purulent masses seen in advanced cases of pulmonary phthisis, and yet I had to examine a number of specimens before I was able to discover a few sparsely scattered bacilli. At the autopsy the lungs were found to be very widely destroyed by the tuberculous process, and vast numbers of bacilli were found in the cheesy foci and the parts surrounding them. Seemingly there is present in the sputum of diabetics, under certain circumstances not yet understood, some substance which rapidly destroys the bacilli—a remarkable contrast to the diabetic tissues which offer so favorable a soil for the development of tubercle bacilli!

2. *Gangrene of the Lungs.*—Pulmonary gangrene occasionally follows fibrinous pneumonia, broncho-pneumonia, injuries to the chest, and even sometimes bronchitis, in cases of diabetes. In other cases

the gangrene appears to occur spontaneously. In general it may be regarded as a rare complication, although more frequent in diabetes than in other diseases characterized by loss of strength and cachexia. It furnishes another evidence of the poor resisting powers of the tissues in diabetes.

IX. Changes in the Circulatory System.

1. *Arteriosclerosis.*[32]—Almost all writers agree that diabetics suffer from premature arteriosclerosis, and therefore are liable to all the troubles, such as cardiac asthma, and exposed to all the dangers, such as apoplexy, degeneration of the heart muscle, peripheral gangrene, necrotic inflammations, etc., which this condition calls forth. Perraro in particular has asserted, and with reason, that arteriosclerosis is the connecting link between diabetes and the parenchymatous glandular degeneration so commonly associated with it. Recently Laache has endeavored to trace a relation between the neuralgias occurring in diabetes and a precedent arterial disease. The arteriosclerosis occurring at a relatively early age sets forth in a most characteristic manner a type of numerous nutritive disturbances in diabetes, viz., premature senile changes. The condition is more marked as a rule in the obese than in those of spare build, and is often far advanced before a diagnosis of diabetes is made.

It is a question that calls for careful study in the future whether arteriosclerosis, possibly of syphilitic origin, may not be often the primary disease which is followed later by diabetes resulting from the nutritive disturbances so occasioned in the pancreas or nervous system. The forms of pancreatic disease most frequently encountered in diabetes, namely, necrosis, fatty degeneration, chronic interstitial inflammation, and atrophy, are precisely the ones which may be caused by endarteritis.

2. *The Heart.*[33]—Reports differ widely as to the condition of the heart in diabetes. Without question there are many patients in whom not the slightest cardiac lesion is present, or in whom the state of the organ corresponds merely to the general nutritive condition of the individual. When disease is present the abnormal deviation may occur in one of two directions:

a. Hypertrophy of the Heart.—In post-mortem examinations of diabetics, O. Israel found hypertrophy of the left ventricle present in 10 per cent. of his cases, I. Mayer in 13 per cent., and Saundby also in 13 per cent. In each case there were at the same time changes in the kidneys, especially true renal hypertrophy. The latter is due to the increased labor devolving upon the kidneys in the elimination of

large quantities of water, urea, sugar, and salts. But O. Israel does not regard this as a sufficient explanation of the cardiac lesion, and he believes that the irritation caused by the excrementitious substances circulating in the blood throws extra work on the heart and thus leads to hypertrophy of the organ. I. Mayer found hypertrophy of the heart in 24 out of 90 cases of diabetes (27 per cent.) during life.

Cardiac hypertrophy in diabetes, as in most other morbid conditions, is a welcome complication; for of itself alone it is never the cause of any distressing symptoms. Nevertheless the muscular tissue of an hypertrophied heart shows a greater tendency than does that of the normal organ to subsequent exhaustion and weakness. The situation differs in no wise from that encountered in valvular troubles, contracted kidney, arteriosclerosis, etc.

b. Cardiac Weakness.—This condition either follows hypertrophy or arises independently of it. Its anatomical basis is often a simple atrophy of the muscle, as has been shown especially by the reports of post-mortem studies made by Frerichs. Associated with the atrophy there may also be fatty infiltration and dilatation. The atrophic heart is naturally found most frequently in those whose general condition is much depressed, especially in those suffering from tubercular complications. Sometimes the etiological factor in weakness and muscular disease of the heart is a sclerotic process involving the coronary arteries.

Clinically weakness of the heart manifests itself in many cases by diminished bodily strength, asthmatic troubles, and a small irregular pulse; in some cases there is a tendency to tachycardia, in others rather to abnormal slowness of the pulse. But, on the other hand, there are cases in which no symptoms of cardiac weakness are present or at least are noticed, until finally with tolerable rapidity, sometimes even very suddenly, paralysis of the organ ensues and the patient dies asphyxiated with all the symptoms of "heart failure." These cases of sudden death have nothing to do with diabetic coma; it is to Frerichs that the credit is due of having made a sharp distinction between the two conditions. The catastrophe occurs ordinarily after some great and unwonted exertion, such as a spell of mountain climbing or a fatiguing journey, or in consequence of some acute psychic disturbance. In view of this fact it is most important to examine with all possible thoroughness the condition of the patient's circulation; and upon the results of this examination will be based the physician's advice as to the amount of bodily exercise which the patient may take.

c. Valvular Lesions.—Valvular insufficiency is often met with as

an accidental complication arising from precedent polyarthritis, etc. At other times lesions of the valves, and then always at the aortic orifices, are found as a result of arteriosclerosis.

d. Neuroses of the Heart.—Cases of functional palpitation and stenocardia are common, being more frequently encountered, however, in individuals of a nervous temperament than in the phlegmatic. They are either a consequence of the fundamentally altered condition of the nervous system or are indirectly due to the diabetes in so far as the latter is the causal condition of the hysterical, neurasthenic, or hypochondriacal troubles. There is no proof of their direct dependence upon the diabetes.

X. Changes in the Kidneys.[34]

1. *Hypertrophy of the Kidneys.*—See page 109.

2. *Granular Atrophy.*—The albuminuria so often observed in cases of diabetes is by no means always a sign of the onset of grave renal diseases; neither is it permissible to refer it to the degenerations of the epithelium to be described below, for the latter belong always to the latest stages only of diabetes. The albuminuria, on the contrary, may appear so frequently in the early stages and without any accompanying disturbances that many writers look upon it as a harmless symptom (Schmitz), although they have never yet succeeded in finding a satisfactory explanation of its origin.

The doctrine of the harmlessness of albuminuria in diabetes must not be established as of universal application, for it not infrequently is in fact a sign of a grave organic disease of the kidneys, almost always then of granular atrophy. It is questionable whether this is directly dependent upon the diabetes itself, the glycosuria, acetonuria, etc., or whether it occurs consecutively to endarteritis. When the granular atrophy has reached a certain stage the glycosuria often disappears, the diabetes is cured, and the further course is that of an ordinary chronic interstitial nephritis. This termination is encountered almost exclusively in the obese and gouty, and practically never in other forms of diabetes.

3. *Glycogenous Degeneration.*—Armanni and Cantani, and later also Ebstein, Perraro, and others, found in cases of diabetes in which death had occurred in coma a peculiar vesicular swelling of the epithelium in the straight tubules and in the descending portion of Henle's tubes. Ehrlich gave the name of glycogen clods (*Glycogenschollen*) to these formations. The nuclei and a portion of the protoplasm of the cells remain. There is probably a resorption of the sugar flowing through the tubules and a conversion of the same into glycogen.

4. *Fatty Degeneration.*—Fichtner has described a collection of fat granules peculiarly arranged in a row in the peripheral parts of the epithelial lining of the convoluted tubes and of the ascending portion of Henle's tubes. The patients had died in coma. Beneke has confirmed this discovery. The relation of neither glycogenous nor fatty degeneration of the renal epithelium to symptoms observed at the bedside has yet been established.

XI. Changes in the Sexual Organs.

1. *In Women* (See above under Pruritus).—(*a*) General rules as to the performance of the menstrual function cannot be formulated. In many women amenorrhœa comes on early in the course of diabetes, in others menstruation occurs at regular or irregular intervals even after the disease has reached a high degree of intensity. (*b*) Conception takes place frequently even in advanced stages of the disease, but in about one-third of the cases the pregnancy is terminated by abortion. During the pregnancy and especially at child-birth the disease is apt to become appreciably worse (see on this point the treatise of Seegen, which contains a good bibliography of the subject). (*c*) The sexual appetite is almost always markedly diminished in severe cases of diabetes, and often indeed changes into an absolute aversion to cohabitation. On the other hand, in mild cases of the disease occurring in elderly women the sexual irritability is sometimes increased to a considerable and even very troublesome degree.

2. *In Men.*—See pages 98 and 103.

XII. Changes in the Lymphatic Glands.

The lymphatic glands, in cases of diabetes, are often swollen and sometimes very markedly so. In severe and rapidly progressive cases, in which the nutrition of the patient is greatly interfered with, this symptom is seldom absent; in mild cases it is often absent. The swollen lymphatic glands are hard and painless, their condition being similar to that seen in constitutional syphilis. But it is certainly not correct to argue from this that any given case of diabetes is of syphilitic origin, although, on the other hand, we are unable to state the cause of the lymphatic swelling. It is very convenient, but unsatisfactory, to refer the condition to the large percentage of sugar in the blood and lymph. It seems to me to be more reasonable to assume that it has some connection with the numerous forms of inflammation of the skin (eczema, acne, furuncles, or the results of scratching). Possibly the tubercle bacillus may play a part in its production.

XIII. Ocular Changes.*

1. *Cataract.*—The opacity, almost always bilateral, of the lens is a late symptom of diabetes and belongs almost without exception to the cases in which there is marked and obstinate glycosuria. The complication attacks by preference young persons, and when it occurs in the elderly is indistinguishable from senile cataract. If the cortical substance of the lens is not destroyed, the cataract usually improves *pari passu* with the improvement of the original disease. The causes of the opacity of the lens were formerly thought to be marasmus, abstraction of water from the lens by reason of the sugar contained in the aqueous humor and in the vitreous body, the presence of sugar in the lens itself, or the change of the sugar held in solution in the aqueous humor into lactic acid. All of these explanations are untenable. Of late we have been taught that a toxic disease of the vessels in the ciliary processes is the cause of the disturbance of nutrition of the lens.

2. *Retinal Diseases.*—Those which are dependent upon diabetes occur under three forms: (*a*) Albuminuric retinitis accompanying contracted kidney present as a complication or sequel of diabetes; (*b*) Retinitis centralis punctata with characteristic ophthalmoscopic changes (small, shining central spots, usually with hemorrhagic puncta, always bilateral, without involvement of the optic nerves; Leber, Hirschberg); (*c*) Retinitis hæmorrhagica of the ordinary type. The retinal diseases are incurable, and are of unfavorable prognostic import. Galezowski found 27 cases of retinitis in 144 cases of diabetes.

3. *Optic Nerve.*—Neuritis, neuroretinitis, retrobulbar neuritis with consecutive atrophy of the optic nerve. These diseases are progressive; they occur more frequently in the severe forms of diabetes than in the milder cases, sometimes as early, sometimes as late, complications.

4. *Amblyopia and Amaurosis, without Ophthalmoscopic Changes.*—As long as these troubles are not of cerebral origin they belong to the early stages of diabetes. They are often the first thing that leads the patient, ignorant of the existence of diabetes, to seek medical advice. The amblyopia appears in the narrowing of the visual field, hemianopsia, or central or paracentral scotoma in an almost normal visual field; in the latter case the affection resembles the so-called

* I follow here in general the statements of M. Knies, in his treatise entitled "Die Beziehungen des Sehorgans und seiner Erkrankungen zu den übrigen Krankheiten des Körpers," Wiesbaden, 1893; pp. 452 *et seq.*

intoxication amblyopia, especially that due to the abuse of tobacco. It would appear, moreover, that many cases are actually to be referred to nicotine poisoning, which occurs more readily in the diabetic than in the healthy organism. These troubles, due for the most part to retrobulbar neuritis, do not readily yield to treatment.

5. *Ocular Muscles.*—According to Galezowski, paralysis of the ocular muscles occurs in seven per cent. of the cases of diabetes; the muscles of accommodation and the external rectus suffer with especial frequency and early. Mauthner considers hemorrhage in the nuclear region, perhaps also at the base of the brain, as the immediate cause of the paralysis. Disease of the vessels is therefore, according to this theory, to be regarded as the connecting link between diabetes and these paralyses. Others, doubtless more correctly, look upon peripheral (toxic?) neuritis as the cause.

6. *Other Ocular Troubles.*—Iritis, iridocyclitis, spontaneous myopia (due to distention of the lens in the early stage of juvenile diabetic cataract or to softening and stretching of the sclera), opacities of the vitreous body (from hemorrhage), recurring scleritis, pustular and ulcerative processes of the cornea, ciliary border, or lids (due to increased vulnerability of the parts), and neuroparalytic keratitis may be simply referred to as comparatively rare phenomena related directly or indirectly to the original disease.

XIV. Changes in the Organs of Hearing, Smell, and Taste.

Change in these organs of special sense play a very subordinate rôle in diabetes, and have received but little study. Weakness or even total loss of function has been noted in each of these sensory spheres, but such complications are of rare occurrence; Frerichs, indeed, has never encountered them. In cases in which central disease of the brain, or, as I have recently observed, complicating hysteria is not present, then neuritic processes must be regarded as the cause of the trouble. Other diseases of these organs can hardly stand in any direct etiological relation with diabetes.

XV. Changes in the Nervous System.

1. *Psychic Disturbances.*—We have seen in the section on Etiology that a clear insight into the significance of psychoses in the causation of diabetes is wanting. We know more, however, concerning the psychic disturbances which arise during the course of diabetes, and which are referred to a nutritive disturbance produced by the original disease in the psychic organs. The question of the diabetic psycho-

ses originated in France, and it is in that country that most of the work in it has been accomplished. In the first rank among these workers are to be mentioned Maréchal de Calvi and Legrand du Saulle. The mental changes which are observed in the course of diabetes are characterized by a tendency to improvement running parallel with improvement in the primary disease and especially in the general condition of nutrition; the fully developed psychoses offer, however, an exception to this rule, for the prognosis in such cases is unfavorable. Occasionally the peculiar fact has been observed that the glycosuria has subsided with the appearance of the mental disturbance and has then remained permanently absent.

The variety and degree of these disturbances vary greatly. Sometimes the symptoms are the common ones of depression of the intellectual faculties and a weakness of judgment, memory, and will; very often there is a tendency to deceitfulness and aimless garrulity; very frequently there are also neurasthenic, less commonly hysterical troubles. The occurrence of actual psychoses is much less common; among these melancholia and hypochondriasis are the first in order of frequency, being observed in all grades of severity from an almost imperceptible degree of mental hebetude to the most pronounced forms of the disorder. Melancholia of diabetic origin frequently presents a homicidal or suicidal tendency. Sometimes there are periodical attacks of somnolence (Ballet, Vergely). Legrand du Saulle has described several cases of "*délire de ruine*" which he regards as very characteristic of diabetic insanity; the patients believe and maintain without any reason that they are financially ruined and this notion dominates all their thoughts and actions. Cases of this nature have hitherto been described only by French writers.

2. *Diabetic Coma.*[37]—This condition was first described by Kussmaul in 1874. It is now generally attributed to the action of some toxic substance upon the central nervous system. I have spoken above of the chemical basis of the various theories held, and have there stated that we have to deal with hypotheses only and have no certain knowledge of the subject, and further that all acute terminations of diabetes associated with loss of consciousness are not identical with true diabetic coma. We have already referred to the cases of sudden death, due, according to Frerichs' opinion, to paralysis of the heart, and we must also distinguish the comatose conditions occurring in diabetes as a consequence of cerebral apoplexy, of the not very uncommon cases of tubercular meningitis, and of other gross anatomical lesions of the brain. Finally many instances of a terminal comatose condition are undoubtedly caused by uræmic intoxication resulting from the complicating contracted kidney.

After all these complications are excluded there still remain a not inconsiderable number of cases of a peculiar character.

Sometimes suddenly, sometimes after headache, insomnia, restlessness, anxiety, vertigo, and symptoms resembling those of alcoholic intoxication, lasting for a few hours or days, the patients fall into a condition of somnolence which rapidly or more slowly passes into complete coma. The patient now lies quietly in bed without any convulsive movements or at most only slight clonic twitchings. The pupils are dilated, the eyes are half-open or the lids are slowly raised and lowered; the eyeballs seem also to move slowly in different directions. The pulse is small and slightly accelerated; the temperature may be at first elevated but sinks later far below the norm. Especially characteristic is the deep, long-drawn inspiration, without stridor, followed by a short expiration; the number of respirations is normal or slightly increased. In spite of extensive aeration of the lungs a slight, gradually increasing degree of cyanosis arises—due apparently to obstruction to the peripheral circulation. A sharp acetone odor issues from the mouth of the unconscious patient and makes a diagnosis of his condition possible even at a distance. The urine gives almost constantly a marked reaction with chloride of iron, and contains sugar; still it must be remembered that the urine of a patient in diabetic coma may be free from sugar (see p. 86).

In this condition, which is only exceptionally interrupted by a brief return of the reflexes and of a clouded consciousness, and even more rarely ends in recovery, the patient remains for from twenty-four to forty-eight hours, seldom longer. Then comes death preceded by a further depression of the temperature and by a gradual diminution in the number and depth of the respiratory movements. Examination of the brain post mortem shows the presence of no lesions to account for this condition.

Frerichs saw 250 fatal cases of diabetes out of a total of 400, and of this number coma was the cause of death in 151; other statistics show a much smaller proportion. Coma may terminate any case, whatever its degree of severity, yet patients with obstinate glycosuria are in very much greater danger of this complication than are those in whom the glycosuria yields readily to appropriate treatment. Most cases occur in patients between twenty and forty years of age.

The cause of the coma is often impossible to determine. The patients are surprised by it without any unusual objective or subjective symptoms having given warning of its approach. The occasional exceptions to this rule in the shape of acute intestinal catarrh or obstinate constipation have already been mentioned (page 105). More frequently the attack is preceded by severe bodily exertion,

excesses *in baccho et venere*, intellectual overwork, or mental excitement. The numerous exact and indisputable observations on this point suggest the thought that we may not always have to deal with coma as a "specific diabetic intoxication" (Frerichs); they would indicate that coma may be often only the expression and the result of a condition of extreme nervous exhaustion. The central nervous system of a poorly nourished diabetic works evidently without any available reserve force. Every weakening movement, every overexertion brings paralysis in its train and gives rise to a condition similar to that resulting from an acute cerebral hemorrhage (apoplectic coma). There is nothing of special significance in the coexistence of marked acetonuria and diaceturia, for they but give expression to the character of the primary disease; it would be remarkable if they were absent. There need be as little question of a peculiar intoxication here as there is in apoplectic cases. It is natural enough that the apoplectic should frequently recover from the shock to the central nervous system, while the diabetic does not. The former is essentially endowed with powers of resistance, the latter is a greatly weakened person. But it is not intended to deny by this that there are forms of coma referable to a genuine diabetic intoxication. Those cases especially belong to this category in which for a long period there has been an excretion of oxybutyric acid.

3. *Brain and Spinal Cord.*[38]—*a.* Symptoms without Central Lesion.—In certain rare cases of diabetes we encounter symptoms which we are accustomed to refer to disease of the central nervous system, such as hemiplegia, aphasia, hemianopsia, and localized convulsions (resembling those of Jacksonian epilepsy). These disturbances may subside or they may lead to a fatal issue. But in the latter case the post-mortem examination reveals no central lesion and no disease, or at most a very insignificant one, of the vessels. The cases recall certain rare forms of uræmia, the phenomena of encephalopathia saturnina, the paralyses without anatomical lesion found in pellagra, etc., and appear to be of toxic origin. Lépine and Redlich have reported cases which may be cited as examples of this condition.

b. Central Lesions.—Diseases of the brain and spinal cord due to a central lesion or system diseases are hardly ever immediately dependent upon diabetes. If they coexist with diabetes it may be that they play a causative rôle or they may be entirely unconnected with it. An indirect relation between diabetes and such affections may be traced in several ways: (1) Through the establishing of an hereditary predisposition, for diabetes has a certain predilection for individuals with a neuropathic taint; (2) through the intervention of disease of the vessels excited directly or indirectly by diabetes (see p. 109), and

leading finally to hemorrhage, softening, etc. Many instances of this sort are recorded in the literature of diabetes; (3) through the agency of syphilis. We have shown that syphilis may under certain circumstances stand in a causal relation to diabetes, and we know on the other hand what an important part syphilis may play in the production of diseases of the brain and spinal cord; (4) through infectious diseases whose occurrence is favored by diabetes, and in the course of which metastases may take place from the local foci of disease to the brain (tuberculosis, suppuration, aphthous stomatitis).

4. *Peripheral Nerves.*[39]—The peripheral nerves are especially prone to disease in diabetes. This fact has been recognized only during the past ten years; prior to that time it was thought that there must be some central disease to account for the manifold sensory, motor, and trophic nervous disturbances observed in diabetes. The last exponent of this view was Althaus, who has set forth at length the differential diagnosis between genuine locomotor ataxia and diabetic pseudotabes.

a. Neuritis. — The most important form of peripheral nervous disease is neuritis, which may appear under the guise of multiple neuritis involving wide areas or be limited to single nerves. Its significance, especially in respect to sensory disturbances (neuralgias, paræsthesias) in diabetes, was first correctly appreciated by von Ziemssen. Soon after this R. von Hoesslin had the happy inspiration to refer the other ataxic affections (see below) to neuritis and to draw attention to the similarity of the symptom complex to that seen in multiple neuritis of alcoholic origin. Since that time the doctrine of toxic neuritis or polyneuritis diabetica has won general acceptance, especially since Auché and others have confirmed the clinical diagnosis by the results of post-mortem examination.

Among the neuritic symptoms encountered in the course of diabetes are: (1) Sensory Disturbances. These are the earliest and in milder cases the only neuritic symptoms; they are paræsthesia, hyperæsthesia and anæsthesia of varied degree and location, pains and cramps in the calves of the legs, and neuralgia. The latter is commonly symmetrical, especially when it is located in the third branch of the trigeminal or in the crural nerves. The diabetic neuralgias are often very obstinate and very painful; they are not, however, incurable. (2) Motor disturbances are not usually very prominent in comparison with the pronounced sensory troubles; still there are cases in which they gain the upper hand and reach a high degree of severity. There is often simple ataxia, or there may be actual paralysis with atrophy and the reaction of degeneration. The paralyses affect the lower extremities much more commonly than the upper, the crural

nerve being the seat of election; they are bilateral as a rule. Of the cranial nerves the abducens is the most frequently affected, less often the oculomotor, hypoglossus, and spinal accessory nerve. The rectum and bladder are never involved.

b. Vasomotor Disturbances.—The affections in this group, local hyperidrosis, local œdema, local asphyxia, and erythromelalgia, are of rare occurrence.

c. Trophic Disturbances.—Among these are localized atrophy of the skin, glossy skin, thinning and shedding of the nails, falling out of the teeth without precedent disease of the jaws, herpes, pemphigus, and spontaneous gangrene, so far as the latter is not due to pre-existing arteriosclerosis.

d. Tendon Reflexes.—Bouchard was the first to call attention to the fact that the patellar tendon reflexes are often absent in diabetes. I find the following statistics relating to this point: The absence of the tendon reflex was noted by Bouchard in 37 per cent., by Maschka in 30.6, by Auerbach in 35 to 40 per cent., by Eichhorst in 21, by Marie and Guinon in 37.5, by Nevière in 40, by Williamson in 50, and by Grube in 7.6 per cent. Very frequently the abolished reflex was observed to return at a later period. There is no relation between this symptom and the severity of the general symptoms of diabetes, for while the reflex may be abolished in mild cases and early in the course of the disease, it may, on the other hand, be preserved in cases of extreme gravity, during coma, and in the agony (Williamson, Grube). It is therefore of no value in a prognostic sense (Rosenstein, Grube). Inflammatory or degenerative changes in the crural nerve have been regarded as the cause of the loss of the patellar tendon reflex.

One or other of the above-described neuritic symptoms is present in almost every case of diabetes; the individual symptoms may appear singly or in groups, and it is to little purpose to attempt to distinguish various types of multiple diabetic neuritis according to the grouping of the symptoms. One thing only is to be noted: The disturbances of sensation, of motion, and of reflex excitability, when present in marked degree, are grouped together in a complex which recalls that of tabes. I have already remarked that special services have been rendered by Althaus as regards the symptomatology, and by von Hoesslin as regards the proper significance of this morbid picture.

The neuritic symptoms appear in part very early, and may be among the first troubles complained of by the patient; this is especially true of the changes in the nerves of the eyes and of the neuralgias. On the other hand, the more severe and wide-spread neu-

ritic affections belong usually to the later stages of the disease. In general they are more commonly associated with the severe forms of diabetes, in which the nutrition of the patient is markedly interfered with, than with the lighter forms, yet it is impossible to establish any direct relation between them and the intensity of the glycosuria. A repression of the glycosuria by the institution of a suitable diet often has a beneficial effect, but in other cases it has no influence whatever upon the course of the neuritis.

GENERAL SYMPTOMS, COURSE, AND PROGNOSIS.

When one considers the immense number of symptoms which may be grouped around the characteristic disturbances of metabolism in diabetes, it is evident that even the most skilful pen would be powerless to draw an altogether satisfactory picture of the disease. Still it may be possible to depict a few types among the many different forms which diabetes may assume.

I. Cases with Acute Onset.

The patients assert positively that the quantity of urine became suddenly greater at a definite period, that they were obliged to rise in the night to pass water, that they suffered from great thirst and hunger, and that, despite the large quantities of food taken, they lost flesh rapidly and failed in strength; to these symptoms were added insomnia, nervous irritability, and generalized pruritus. Usually in these cases it can be ascertained that the patient had suffered from some great psychic disturbance or a bodily injury. Almost always the patients are young and the family history presents many cases of diabetes or some other constitutional disease.

The intensity of the glycosuria at the beginning in these cases furnishes no data upon which we can base a prognosis or judge of the subsequent course of the disease, but after a short time (a few weeks or months) matters usually shape themselves in such a way that we can form a pretty accurate estimate of the gravity of the case.

1. If during this interval the sugar-consuming function becomes essentially better, the case will almost always result in recovery; at first the urine becomes sugar-free after the withdrawal of carbohydrates from the food, and later the carbohydrates are tolerated in increasing amounts until a permanent cure is effected. Schmitz describes several cases of this kind, and F. A. Hoffmann had this form of the disease in mind in his characterization of neurogenous diabetes (see p. 71). The sooner the carbohydrates are withheld the better will be the prognosis. Cases of this kind are unquestionably rare.

2. If the tolerance of carbohydrates does not become materially greater after the patient has been on a suitable diet for some weeks or months, these cases progress almost without exception to a rapidly fatal termination (within one or two years), even when the glycosuria yields to a strict abstinence from carbohydrates and the nutrition is satisfactorily maintained by a plentiful supply of albumin and fat. A complicating tuberculosis or diabetic coma puts an end to the patient's existence. The other complications are of subordinate importance.

II. Severe Cases with Ordinary Onset and Course.

Here nothing definite can be learned of the beginning of the disease. The bodily weakness, intellectual relaxation, impotence, and emaciation have come on gradually and almost imperceptibly. The patients look upon themselves as nervous and overworked in body and mind. They therefore give themselves a vacation from time to time, visiting the different watering-places and summer resorts, without, however, finding the wished-for return of strength. They even consult a physician occasionally, who frequently, through neglect to examine the urine or because of deficient powers of penetration, fails to detect the true cause and agrees with the diagnosis of overwork, neurasthenia, nervous dyspepsia, and the like. At other times disease of some other organ develops (visual disorders, neuralgia, impotence, pruritus, furunculosis, tuberculosis, etc.) and leads the patient to consult a physician, often a specialist, an ophthalmologist, a dermatologist, a neurologist, or the like. The variety of forms under which the disease appears is but too often responsible for the fact that the diagnosis is made only when sad destruction has already been wrought in the body through defective nutrition, or through complications or sequelæ of the primary disease. A more careful examination shows that the patients are excreting under the ordinary diet rich in carbohydrates, enormous quantities of sugar—200 to 300 grams or more a day. The tolerance of carbohydrates is at a minimum or even negative, that is to say, the glycosuria continues for a time, or it may be permanently, despite the withdrawal of carbohydrates from the food.

The further course of the disease varies.

1. In consequence of proper regulation of the diet as to quality and quantity, good nursing, careful treatment of the complications, avoidance of any tax to the mind or body, the nutritive condition becomes better, the patient increases in weight, his strength returns, he becomes able to perform a moderate amount of bodily or mental labor, the complicating organic diseases improve or at least become stationary, and the tolerance of carbohydrates increases slowly, with oscilla-

tions, to a certain, though usually slight, degree. The patients drag out an anxious existence full of privations for several years, perhaps a decade. The general condition is variable, now good, now bad. Any little careless neglect of the dietetic or other rules which have been established for them is ordinarily followed quickly by a loss of weight and strength. In the mean while complications are not absent; the old troubles (neuralgia, visual defects, furunculosis) return; new ones (digestive disorders, trophoneuroses, mental disturbances, paralyses, cardiac asthma) declare themselves, and the more serious complications (acute infectious diseases, tuberculosis, gangrene, heart failure) appear. Finally the patients succumb either because they are unable to take and assimilate sufficient nourishment to maintain the strength, or because they are overcome by some intercurrent disease, such as heart failure, tuberculosis, or gangrene, or finally because diabetic coma comes on suddenly and unexpectedly.

2. In contrast to these relatively favorable cases are others with rapidly fatal course. The gravity of the cases is betrayed less by the glycosuria than by the other symptoms. The intensity of the former is doubtless also of great significance in so far as the giving of suitable and sufficient nourishment becomes the more difficult in proportion to the depression of the sugar-consuming function. But the cases which we are now considering present the peculiarity that the swiftly advancing fatality is not turned aside even when the dietetic difficulties are victoriously overcome.

In a certain number of these cases the vulnerability of the diabetic tissues is shown to a fearful degree, or precocious senility declares itself. The patients are attacked by severe complications and sequelæ in spite of the best care and of the most painstaking regulations of the mode of living; they suffer from severe forms of neuritis, grave conditions of weak heart, phlegmons, gangrene, and above all tuberculosis. One or other of these complications, or the combined action of several, kills the patient within the short period of one or two years, although in the last stages of the disease the glycosuria may have decreased very considerably and thereby given rise to deceitful hopes of an improvement in the primary affection.

In another proportion of cases the signs of true diabetic intoxication declare themselves, sometimes independently of, sometimes in connection with, other complications. Fatal coma appears, either after a long prodromal period (especially a profuse excretion of oxybutyric acid) or without any warning. By far the greater number of patients who are attacked by this malignant form of diabetes, progressing inevitably to a fatal termination within one or two years, are young or middle-aged.

III. Benign Cases.

The mild forms of diabetes compatible with a long life are by far the most frequent. They belong almost exclusively to the middle and later periods of life, and affect by preference, though by no means invariably, corpulent individuals and those suffering from the gouty diathesis. The manner in which obesity and gout stamp their characteristic imprint upon diabetes has been described in previous sections, to which the reader is referred (see pp. 66, 68, and 71).

The benign cases have certain peculiarities in common. The time of their onset is seldom known. The glycosuria is discovered accidentally or after an examination of the urine suggested by certain complications. Pruritus, furunculosis, disturbances of accommodation, neuralgia, and impotence are the complications most commonly encountered. The glycosuria yields at once to a withdrawal of the carbohydrates from the diet, and usually there is even a certain tolerance of moderate amounts of starch. This tolerance is subject to considerable variations, and often remains at a high figure for weeks and months. A few weeks of strict dieting, intellectual rest, a sojourn in a pleasant locality, and the like, work a marked change for the better, while imprudence in eating, overwork of body and mind, etc., lead to a deterioration in the general condition, insomnia, lassitude, and an increase in the glycosuria. After long years of varying health the tendency to excretion of sugar diminishes as a rule and may even wholly disappear. Not infrequently albuminuria appears, and finally the well-known symptoms of contracted kidney take the place of those of diabetes.

The complications and secondary affections, appearing frequently at the beginning of the disease in mild form, are in its later stages little to be feared with the exception of those conditions which are dependent upon arteriosclerosis, especially peripheral gangrene, cardiac asthma, and apoplexy.

These forms of the disease may, through neglect and gross dietetic abuse, lead to a loss of strength and an unfavorable termination despite their benign tendency. Danger threatens especially on the side of the heart; diabetic intoxication with coma may ensue, but it is rare. The same is true of the transformation into the rapidly progressive malignant varieties.

IV. Intermediate Forms.

There are many intermediate forms between the two extremes just presented, so that only a certain number of cases actually correspond to the typical clinical picture. It is impossible to describe all these

intermediate forms with all their manifold shades and differences. A careful study of the individual case will show which of the two groups it more nearly approaches.

V. General Prognostic Signs.

a. Favorable:

1. Onset of the disease late in life;
2. Long duration of the diabetes prior to the time of observation, no grave complications having appeared in the mean time nor any considerable emaciation having taken place;
3. Traumatic causation of the disease (psychic or corporeal injuries);
4. Syphilitic origin of the diabetes;
5. The occurrence invariably of mild forms of diabetes in the family of the patient;
6. Precedent and coexisting obesity;
7. Coexistent uric acid diathesis;
8. Slight intensity of the glycosuria and tolerance of certain moderate amounts of carbohydrates;
9. Marked oscillations and gradually increasing tolerance of carbohydrates;
10. Comfortable circumstances which permit of the carrying out of the dietetic and general hygienic prescriptions.

b. Unfavorable:

1. Onset of the disease in early life, especially in childhood;
2. Great loss of strength, despite a brief duration of the diabetes;
3. A history of severe forms of the disease in other members of the patient's family;
4. Early appearance of grave secondary diseases and complications;
5. A high degree of intensity of the glycosuria, with complete or almost complete intolerance of carbohydrates;
6. Poor circumstances which render impossible the carrying out of a dietetic treatment or the avoidance of bodily and mental overwork;
7. Excretion of oxybutyric acid; coma.

TREATMENT.

It is not possible to give an exhaustive presentation of the therapy of diabetes mellitus in this place, for its history is long, and it has undergone such manifold changes in the course of time that a mere description of them would fill a large book. I intend, therefore, hav-

ing regard to the space that is at my disposal, to set forth simply the principles of a rational therapy of the disease, entering into details only where points of practical importance arise.

A strong subjective factor enters into every therapeutic ordinance which is established at the bedside. He is a poor physician who asks himself: What do the schools prescribe, what does this or that authority prescribe in the disease with which I have to do? The true physician weighs in his mind his own and others' experiences, but stands in the presence of the patient and of the disease resting upon his own authority, conscious that the responsibility must be assumed by himself alone, whatever weight he may also give to the results of others' experience.

In the capacity of an author I claim the physician's right and the physician's duty in the domain of therapeutics. I shall not enter into an account of "what is done" for diabetes, but shall state only what I myself am accustomed to prescribe and the reasons therefor.

I. Prophylactic Treatment.

We can scarcely say anything of the prophylaxis of diabetes mellitus beyond laying down the most ordinary and every-day rules of a hygienic and health-preserving mode of life. Practically it is only under certain special circumstances that we can have to do with any prophylactic measures. In the first place we may consider those individuals in whose family there is a history of many members being attacked by diabetes in early life. Possibly in such cases the early and permanent withholding of carbohydrates, especially of sugar, from the diet may prevent the occurrence of the disease. But beyond the qualification "possibly" we cannot go.

Then again there may be a question of prophylaxis in the case of those individuals, especially men, who are driven into luxurious living by their social position, who in the prime of life grow corpulent quite rapidly, and in whose family there is a history of many cases of diabetes. Very frequently these three factors are united. I have already given expression to the conjecture that there is a certain disturbance of carbohydrate change in many cases of obesity, even without an accompanying glycosuria. As it is very probable that once an anomaly in respect to sugar conversion has arisen, the ingestion of carbohydrates will make it worse and their withdrawal will improve it (see below), it is advisable to recommend in these cases also a gradual diminution in the amount of carbohydrates in the diet. An over-consumption of carbohydrates will be sufficiently prevented by the prohibition of sugar, farinaceous foods (such as the cereals, pud-

dings, maccaroni, nudels, and the like), pastry, preserves, and sweet champagne, and by the restriction of the daily amount of beer taken (from one to three glasses). Through these dietetic regulations, especially when supplemented by muscular exercise, the further progress of the obesity is arrested or at least retarded; sometimes there is even a gradual loss in weight. I would, however, warn the reader most earnestly against subjecting to an energetic reduction treatment all individuals whose own past or whose family history raises the suspicion of a developing diabetic diathesis. The patients are often thereby weakened and permanently invalided, and the disappearing obesity frequently enough gives place to diabetes.

II. Etiological Treatment.

Are we ever able to institute an etiological treatment of diabetes? Can we remove the cause and therewith the disease itself? Let us see.

1. *Neurogenous Diabetes.*—(*a*) Diabetes Accompanying Functional Nervous Disorders.—If severe mental overwork or psychic disturbance accompanied by marked neurasthenic symptoms have preceded the occurrence of diabetes and appear to have caused it, we shall doubtless be following a most rational therapeutic course if we devote special attention to the treatment of the morbid condition of the nervous system. In such cases, in addition to the dietetic measures and even indeed before their institution, we should endeavor to strengthen the nervous resisting powers of the individual. Before all else we should seek to obtain for the patient relief from confining and exacting professional labors, avoidance of everything that causes worry, and the removal of domestic cares which constitute in themselves constantly renewed causes of uneasiness. Unfortunately our efforts in this direction are often confined to pious wishes. In many cases a long journey in pleasant regions with freedom from business cares suffices to restore the equilibrium of the psychic functions, to raise the spirits, and to banish insomnia. In general a stay in warm dry regions is to be preferred. Sub-alpine summer resorts are excellent for the hot months. Diabetics as a rule do not bear damp cold or raw sea air well, for it increases their nervous irritability and causes great discomfort to those of them who are sensitive to external cold.

In other cases, or perhaps supplementary to the procedures already mentioned, hydrotherapeutic measures are useful. The most advantageous of these for nervous diabetics are prolonged warm baths (tub baths, indifferent natural thermal waters, mud baths), or, still better, baths in which carbonic acid gas is set free. On the other hand,

strong salt baths and especially bathing in the open sea are particularly to be avoided, since they rather fatigue and exhaust than invigorate sufferers from diabetes. Caution must be had also in the use of cold frictions and cold douches; there are certain diabetics to whom these are most serviceable, but others who do not react even after rubbing for half an hour or an hour; they lose their appetite, suffer from sleeplessness, and become very nervous.

As regards the dietetic regulations, which are of undoubted service in other patients of nervous constitution, we are in a delicate position. We have to do usually with spare individuals in whom an improvement in the nutritive conditions is urgently indicated. The attainment of this object is, however, made difficult by the necessity of withholding as far as possible all carbohydrates from the fattening diet. In general we must be guided in our choice of a diet by the intensity of the glycosuria, a subject which will be treated of in a subsequent section. Here, however, we may remark that the more prominent is the neurasthenic state of the patient the less able are we to dispense with the carbohydrates. It is allowable to diminish or even to withhold entirely the carbohydrates temporarily, but never for more than a few weeks at a time.

Concerning drugs there is not much to be said in this place, except perhaps that the skilful use of medicinal remedies gives better promise in the nervous than in other forms of diabetes. The more prominently nervous irritability stands out and the more probable it is that this is the fundamental cause of the diabetes (and also when the nervous disturbance has first declared itself during the course of the diabetes), the stronger is the indication for narcotic remedies. The favorable results which have for many years been claimed for opium administered with a free hand, and more lately for one of its alkaloids, codeine, are to be referred especially to cases of this sort. The remedy quiets the irritability of the central nervous system and exerts in this way slowly and gradually a curative effect. The theory that opiates increase the sugar-destroying power of the tissues seems to me to be wholly unfounded. In any case the opiates are suitable only for temporary use, and they should never be prescribed for longer than a few weeks at a time. Other nervines, such as antipyrin, phenacetin, etc., may be advantageously substituted for them from time to time, but even these remedies are more injurious than helpful if given for long periods. The bromides, on the other hand, can be unhesitatingly recommended, for they can be given continuously for months without harm to the patient, and when administered in suitable cases are of undoubted benefit. One should not, however, look for the impossible, and it should be remembered that the

bromides are not a specific remedy for diabetes, but merely a valuable aid in combating abnormal nervous irritability. For a further consideration of these and other medicinal remedies, see below.

The endeavor to strike at the root of the disease by treatment of the nervous irritability is often crowned with success. It is true that it is only in rare instances that we see a complete and lasting cure, but in many cases we can obtain a decided improvement as manifested by the fact that the previously weak and feebly resistant patient, who responded to every irritation by an increased glycosuria, now excretes much smaller quantities of sugar under the same diet, and is able to meet the problem of life with a firmer bearing and greater capacity. I may say, indeed, that it is this very therapeutic success obtained by acting upon the general nervous system, that forces upon the physician the conviction that there is really a neurogenous form of diabetes.

b. Diabetes Accompanying Organic Nervous Diseases.—The conditions present in organic disease of the nervous system are much less favorable than those just considered. We have seen above that it is almost without exception the brain and medulla oblongata that are affected in these cases. We do not refer to the transitory glycosuria following trauma, apoplexy, and the like, which disappears at the end of a few hours or days. It is very improbable that we can ever prevent, by any therapeutic measures at our command, the transition of temporary glycosuria into chronic diabetes.

But it seems to be certain also that diabetes mellitus of weeks' or months' duration, which has followed a cerebral injury, concussion of the brain, sunstroke, etc., may often subside spontaneously and coincidently with the improvement in the nervous affection (F. A. Hoffmann). It would seem to be a thankful task of therapeutics to follow in the path pointed out by nature, but in fact real benefit from active therapeutic measures in organic diseases of the brain is obtained only in those few cases to which surgical procedures are applicable, and in cerebral syphilis. We know of no instance, however, in which a chronic diabetes has been cured as a result of the extirpation of an intracranial lesion, of an operation upon a hæmatoma of the dura mater, a brain tumor, an abscess, or a hydrocephalus externus or internus, or of the mercurial treatment of a gummatous meningitis or encephalitis. The future alone can show whether the path here pointed out will lead to any practically useful results. Any positive successes in this field would be also of striking significance in respect to the theory of diabetes.

2. *Syphilitic Diabetes.*—It has been shown above that syphilis may lead to diabetes in either of two ways: (*a*) Through the in-

tervention of cerebral disease; this is apparently very rare, and the fact meets us that no case is known in which a cure of diabetes has been obtained indirectly by a previous cure of cerebral syphilis; (*b*) through the intervention of syphilitic disease of the pancreas.

I have shown that this may possibly play a more important rôle than has hitherto been attributed to it in the text-books on special pathological anatomy. We cannot ignore the positive assertions of certain writers that they have seen cases of diabetes improved or even cured by mercury and iodine. Schnée records no less than 53 cases of cure and 10 of improvement out of a total of 74 treated by mercury. Seegen also reports some successful cases but says that they are rare. I have known personally of perhaps a dozen cases in which syphilis preceded the occurrence of diabetes; a cure was obtained in no instance, marked and lasting improvement in but two, by mixed treatment with mercury and the iodides; in several instances fatal complications followed the use of mercury—once gangrene of the foot, twice hæmoptysis and rapid progress of the already incipient tuberculosis of the lungs. It is hardly possible to form a positive judgment as to the practical value of the antisyphilitic treatment of diabetes. Whoever undertakes it must have the patient under control and see him every day, for diabetics are very prone to suffer from mercurial stomatitis and from a mercurial intestinal catarrh with symptoms resembling dysentery. The best mode of administration of mercury in cases of diabetes is by inunctions carefully made and supplemented by frequent baths.

III. Methods of Increasing the Sugar-Destroying (Glycolytic) Function.

It was shown in the preceding section that the removal of the causes leading to diabetes can seldom be attempted with hope of success. If these attempts are not successful, whether because the cause is out of the reach of our therapeutic measures, or because the diabetic changes have become independent of the cause, or finally because, as is usually the case, the cause is unknown, the question arises whether we possess any means of increasing the sugar-destroying energy of the organism. In this direction, indeed, we are not altogether powerless.

1. *Treatment with Pancreas Preparations.*[40]—I begin with the consideration of this form of treatment, in spite of the fact that its practical results have been very insignificant, for the theoretical interest which it has aroused is great and increasing. It is based upon the assumption that the pancreas furnishes by its internal secretion a

material necessary to the function of normal sugar consumption (see p. 53). We may recall in this connection what is seen in the case of myxœdema; here there is a defect in a gland (the thyroid) as regards its internal secretion, with serious results to the organism; and apparently brilliant effects are obtained by the administration of the juice or extract or of the substance itself of the thyroid gland. What then was more probable than that similar results should be obtained in diabetes? This was a question that could be determined only by experiment, for it might well be that the active material is formed only at the moment of its secretion and is not to be found in the gland itself.

The experiments thus far made have been partly with raw pancreas mixed with the food, and partly with aqueous, alcoholic, or glycerin extracts of the gland administered by the mouth or subcutaneously. The results have not been satisfactory; no actual cures have yet been obtained, but some instances of temporary improvement have been reported by individual writers; they are not sufficient, however, to warrant a belief in the future of the method. I can only agree with Fürbringer, Leyden, and Goldscheider in withholding judgment for the present. The method is nevertheless worth further trial, and should be employed especially in those cases in which there is good cause for regarding the pancreas as the seat of the disease.

2. *Treatment by the Withdrawal of Carbohydrates.*—We have seen that reducing the supply of carbohydrates causes a diminution of the glycosuria. In some cases complete abstinence, in others a greater or less reduction of the amount of carbohydrates ingested is necessary in order to arrest the glycosuria; in other cases again the condition persists in a slight degree in spite of the total withdrawal of saccharine and starchy foods. But it is, in any case, a mere concealment, as it were, of the diabetes; if carbohydrates were taken again the glycosuria would reappear in all its former intensity.

The important discovery has, however, been made that something more than this is obtained by the diminution or total withdrawal of carbohydrates. Individuals who have been for a certain time (several weeks) on a diet containing no saccharine or starchy ingredients often acquire a tolerance of carbohydrates, and excrete much less sugar after the ingestion of a certain quantity of amylaceous food than they did before. This fact has been especially emphasized by Naunyn, who says that the sugar-consuming function of the body is spared by the temporary withdrawal of carbohydrates and is thus given an opportunity for recovery and restoration of strength. Naunyn,[41] as well as his pupil Weintraud, confirms this teaching by such convincing examples that all doubt is silenced. In severe cases of glycosuria the

success of measures directed toward an increase of tolerance is very slight and evanescent, in those of moderate severity it is better, and in mild cases it is often excellent, most evident, and lasting. After having thus explained the principle upon which this method is based, we shall see later how we can best avail ourselves of it in practice.

3. *Treatment with Mineral Waters.*—Here we have to consider: (*a*) simple alkaline waters, such as those of Assmanshausen, Neuenahr, Salzbrunn, Vichy, etc.; (*b*) alkaline sulphur waters, such as those of Bertrich, Carlsbad, Marienbad, Tarasp, etc.; and (*c*) saline waters, such as those of Homburg, Kissingen, Salzschlirf, etc. Those of the first two groups are the most frequently employed, the saline waters—perhaps wrongly—being used less often. Adjuvants to the treatment at these resorts are the pleasant surroundings, much time spent in the open air, freedom from domestic cares, diminished supply of carbohydrates, and a proper amount of bodily exercise together with the regulated use of the waters. It is a fact that in many cases of diabetes the tolerance of carbohydrates is so increased by this therapeutic regimen that the patients find, after returning to their homes, that the ingestion of equal amounts of carbohydrates is followed by a much less marked increase of glycosuria than before. These results are especially and most strikingly observed in the mild forms of glycosuria occurring in obese or gouty subjects. For these cases the alkaline sulphur waters are in most favor, but it seems to me that for weakly and anæmic diabetics, who need to be spared in every way possible, the mild saline waters (at the head of which are Kissingen and Homburg) should be given the preference. On the other hand, for very irritable, neurasthenic patients of spare build, and further where gout is accompanied by marked nervous irritability, the simple alkaline waters are better suited.

The results of this treatment are incomparably less, absolutely as well as relatively, in the severe forms of glycosuria. Such patients usually return home without any increase of tolerance for carbohydrates, often enough with even diminished tolerance. The greater the intensity of the glycosuria, the more useless and even injurious are the alkaline and alkaline sulphur waters. There must be a considerable resisting power in order that mineral-water cures may be well borne and do good. Very young, aged, and greatly reduced diabetic patients are out of place in these spas. The latter suffer from digestive disturbances and heart weakness either at once or soon after their return home. Caution is demanded also in cases in which nephritis exists as a complication, for after the use of the waters of Carlsbad or Marienbad a previously harmless nephritis (granular atrophy) often begins to grow rapidly worse. The muriatic and

alkaline muriatic waters are much better borne by diabetics with nephritis.

In this matter experience is our only guide. Why Carlsbad and other similar waters should act so favorably under certain circumstances, we cannot explain theoretically. It is difficult also to appreciate the part taken by the individual factors in the general plan of treatment employed at these baths (see above), and to arrive at any definite assurance that an essential part of the treatment consists in the use of the mineral water itself. Nevertheless, resting upon the ground of experience, we cannot doubt that such is the case. What is attained in suitable cases is certainly more than an apparent result; there is an actual increase in power of the sugar-destroying function.

4. *Medicinal Treatment.*—The number of drugs which have been recommended in the treatment of diabetes is legion—an evidence of the small benefit of any individual one. Even the most optimistic believers in materia medica, rendered cautious by oft-repeated disappointments, become sceptical when any one praises a remedy for diabetes. The question is not whether many drugs are not useful and even necessary in diabetes in order to meet one or another of the special indications or to combat the complications, but rather whether we possess any remedy which can increase the energy of the sugar-destroying function. It often seems as though we did possess such a remedy. I have already shown that the glycosuria may become less pronounced after the use of many drugs classed as nervines, such as opium, codeine, bromide of potassium, antipyrin, phenacetin, antifebrin, exalgin, sulphonal, thallin, valerian, belladonna, etc. I added also that the action of these remedies was probably an indirect one, since the condition of nervous irritability was first improved, the decrease in the intensity of the glycosuria being secondary.

It is out of the question to present here a complete list of all the old and new preparations which have been recommended from time to time, whose popularity has been for the most part very ephemeral. The following are a few only of these drugs: Salicylic acid, benzoic acid, salol, benzosol, guaiacol, creosote, turpentine, tincture of iodine, the iodides, oxygen, ozone, permanganate of potassium, lactic acid, strychnine, brewers' yeast, quinine, iron, arsenic, pilulæ myrtilli Jasperi (whortleberry), and testicular juice. I do not doubt the trustworthiness of those who have reported favorable results from these drugs, but I myself have never observed any effect when I adhered strictly to the rule of making no change whatever in the diet either before, during, or after the administration of the remedy under trial. I cannot help thinking that in many cases the successful result is due

to suggestion. Diabetics are very fond of trying new methods of treatment, and the belief that they will be helped by the new cure gives great comfort to many of them; their self-confidence is increased, worry diminishes, sleep returns, and the subjective symptoms are improved—and all of these are unquestionably factors of far-reaching importance in regard to the glycosuria in nervous diabetics. We do not understand the connection, but are compelled to recognize it.

In many cases syzygium jambolanum (the bark and seeds of the Java plum) appears to have a more direct action. Personally I have never seen any results worth mentioning from the use of this drug, but the many cases on record in which good results have been obtained cannot be ignored. Perhaps in the course of time we shall learn to distinguish the cases in which a diminution of the glycosuria may be expected from the use of syzygium and those in which no such result can be looked for.

I do not deny, as may be gathered from what has been already said, that something may be accomplished by drugs, and I freely admit that by their employment we may pass beyond the limits of symptomatic treatment and may directly or indirectly exert a favorable influence upon the main disease. But that every rational or empirical indication for the medicinal treatment of the abnormal metabolism of diabetes is wanting is a fact that rests on a much firmer basis than does this concession. When we prescribe any drug in diabetes we are groping in the dark, and must learn by experience in each individual case whether we are following the right path or not.

Having regard to the uncertain basis for medicinal treatment and to the manifold by-effects of the drugs employed, the administration of medicinal remedies should be undertaken only when the physician is in position to control their action by careful observation of the general condition and of the glycosuria. Poisonous substances, such as opium, codeine, antipyrin, salol, etc., should be administered for long periods only when a favorable action is very evident, and it is unjustifiable to prescribe any of these drugs unless the patient can be kept under constant surveillance—indeed, to do so would be little short of malpractice.

IV. Hygienic and Dietetic Treatment.

In view of the lack of appropriate remedies by means of which we can attack the course of diabetes or increase the energy of the glycolytic function, the hygienic and dietetic treatment of the disease is deserving of the most careful consideration. Much that is to be discussed here has already been referred to, as we have had to

consider the hygienic and dietetic factors in order to arrive at a comprehension of the subjects treated of in previous sections.

1. *General Considerations concerning Diet in Diabetes.*

a. Preservation of the Body Albumin; Calorie Value of the Food.—*Under all circumstances, the diet in diabetes must be so ordered that the strength of the patient may be thereby maintained and as far as possible increased.* As the strength depends essentially upon the stability of the body albumin, that is to say, of the tissues which contain it, the blood, glands, and muscles, the above condition, translated into the language of the doctrine of metabolism, would read: The nourishment supplied to the patient is to be so ordered that the store of albumin in the body may remain stationary or even be increased.

Fat, which represents only dead fuel, may when necessary be sacrificed; in spare individuals of course as little as possible, but in the obese by preference. Nevertheless, it must be remembered that energetic and rapid reduction of adipose tissue is as a rule badly borne by diabetics. Any diet which is not adapted to assure the maintenance of the diabetic's store of albumin is in my opinion unsuitable for long-continued use; it may be employed temporarily, but as a permanent thing it is objectionable and dangerous.

In order to insure the preservation of the body albumin an amount of food adapted, in accordance with general physiological laws, to the needs of the organism is necessary. If the amount sinks below these needs, that is to say, below the output for the time being of the organism (dependent upon the weight of the body, the loss of heat, work done, etc.), the deficit must be met by a destruction not only of the fat but always also of the albumin of the body. The only exception to this is in the case of corpulent individuals, for whom, regard being had to certain necessary precautions, the diet may be so regulated that waste of albumin stored in the body does not take place (von Noorden and Dapper [42]).

We know that a grown man, taking moderate exercise, consumes nutritive material to the value of at least 35 calories per kilogram a day (see p. 87). Spare individuals consume somewhat more, fat persons considerably less. In the case of a man of average weight, say 70 kilograms (154 lbs.), the average of the daily consumption would be represented by about 2,500 calories.

I think it is expedient to take this figure as the standard in our further considerations. Of course the reservation must be made that this is only an average which is to be changed according to the body conditions present (size, amount of adipose tissue, weight, age) and

according to whether the individual leads an active or sedentary life. With this reservation I would formulate the following proposition:

The diet of the diabetic must be so constituted that it will furnish available material to the value of at least thirty-five calories per kilogram per diem.

b. The Depreciation of the Carbohydrates of the Food through Glycosuria.—In order to obtain the necessary amount of nutritive values the healthy individual must make use of the carbohydrates in very considerable quantity. In most men they meet 40 per cent., and often much more, of the entire daily nutritive requirements. But the carbohydrates, of the greatest value for the healthy man, are for the diabetic a nutritive material of subordinate rank, since they are excreted in part unused in the urine. The greater is this part the more worthless are the carbohydrates as a building material and the more must they be regarded as mere waste matter in nutrition. The difficulty of affording nourishment to the sufferer from diabetes is therefore increased in inverse proportion to the tolerance of carbohydrates. While in the case of one diabetic we are able to give such an amount of carbohydrates that, although a certain small proportion is lost in the urine, the large remainder suffices to cover a quantitatively important part of the daily tissue change, in another no advantage worth mentioning accrues from the ingestion of carbohydrates, give them in what quantities we will. For example:

Diabetic A. Carbohydrates of the food, 200 grams = 820 calories.
" in the urine, 20 "
Available for the body, 180 grams = 738 calories.

Diabetic B. Carbohydrates of the food, 200 grams = 820 calories.
" in the urine, 180 "
Available for the body, 20 grams = 82 calories.

As the sugar which escapes in the urine is lost to the economy, the same food has a very different calorie-value for the healthy and for individual diabetics. For instance (see the example given on page 87):

150 grams	albumin	=	615 calories.
100 "	fat	=	930 "
200 "	carbohydrate	=	820 "
	Total.....		2,365 calories.

Value of this diet for the healthy individual, 2,365 calories.
" " " " " Diabetic A. 2,365 — 82 = 2,283 calories.
" " " " " Diabetic B. 2,365 — 738 = 1,627 calories.

This presentation shows that the depreciation of the nutritive value of the food by reason of the sugar waste, varying in each individual case, is to be taken into consideration in prescribing the quantity of nourishment; it teaches further that, the greater is the intensity of the glycosuria, the more must the patient look for the support of his strength to other nutritive materials, proteids, fats, and, in moderate quantities, alcohol.

We may also remember that certain forms of carbohydrates are more suited to the diabetic's use than are others,—for example, fruit sugar, milk sugar, and in certain quantity also cane sugar. In practice, however, the advantage derived from their use does not meet our theoretical expectations. In mild forms of glycosuria occurring in elderly people very little depends upon the variety of the forbidden carbohydrate, and in the severer forms the gain in available carbohydrates is only a little greater, even when large doses of fruit sugar, milk sugar, and the like are given, than with the use of bread and farinaceous foods. The disadvantage of glutting the organism with carbohydrates might easily overbalance the gain in utilizable nutritive material. On the other hand, in cases of moderate severity and in mild forms of glycosuria in young people, these special forms of carbohydrate, with milk sugar at the head, seem to me to be worthy of the practitioner's special consideration (see below, in the section on "Milk-Cures").

c. The Injuriousness of the Carbohydrates.—Under certain circumstances carbohydrates are injurious to the sufferer from diabetes. It will be well to define these circumstances more exactly, as many confusing opinions have been expressed on this point.

It is not alone that carbohydrates are of little value in the severe forms of glycosuria, their ingestion being comparable to pouring water into a cracked vessel, but large quantities are even harmful in grave cases. Many attribute the injurious consequences of the ingestion of carbohydrates to the increased percentage of sugar in the blood, and refer the secondary affections of all kinds, occurring in the diabetic, to this condition (*cf.* p. 100). I have already said that this hypothesis is anything but well founded. But it is a fact that diabetics who indulge freely in carbohydrates, without regard to the severe glycosuria present, suffer in the course of time from a markedly decreased tolerance of starch and sugar. They react to the same amount of carbohydrate taken in the food by a more intense glycosuria than before. This observation can be easily made in almost all severe cases, and the reverse of it, an improvement of the glycolytic function following a reduced ingestion of carbohydrates, may also be adduced in support of this statement. This fact is explained by

the general biological experience, which has been demonstrated with special clearness by F. A. Hoffmann, that functionally weak organs (in this case the sugar-consuming cells) are injuriously affected and made yet weaker if continuously spurred on to overwork. Rest, not exercise, is for them the proper treatment.

From this point of view it would be best in cases of considerable or extreme severity (tolerance = 0 gm. or < 0 gm. carbohydrate) to strike the carbohydrates entirely out of the food; it is only a concession which we make to other evils when, in these cases, we allow a certain amount of carbohydrate either temporarily or permanently. The reasons which constrain us to yield this point will be considered in the next section.

From the same point of view, however, we are not compelled to banish the carbohydrates entirely in those cases in which a certain degree of tolerance for them exists. Here we have to regard the sugar-consuming function only in so far as to see that it is exercised within the limits of its capacity. When, for example, a patient excretes no sugar while taking 50 grams of bread, and perhaps 10 grams of sugar while taking 100 grams of bread a day, we can then permit him, with a good conscience, to eat from 50 to 100 grams of bread. Experience has taught us that we need have no apprehension even if we exceed a little the limits of tolerance in these cases; it is only a glutting of the organism with carbohydrates that we must avoid.

But this question of overtaxing or sparing the sugar-destroying function is not the only one that calls for medical control and for a reduction in the amount of carbohydrates ingested. Another way in which harm results is that the patient, if left to himself, may easily take so much carbohydrate, which is of but little use to him, that the other and valuable nutrient substances, the proteids and fat, fall short; he eats and gorges, yet is not sufficiently nourished. The stomach is satisfied but the tissues are starved; the patient emaciates, loses strength, and becomes predisposed to secondary diseases. As soon, however, as his diet is regulated, the ingestion of sufficient quantities of albumin and fat is prescribed, and the carbohydrates are relegated to a subordinate position, being allowed, as it were, as a reward for his conscientious adherence to the main diet; then the strength returns and he becomes once more, instead of a miserable, weakly invalid, a useful member of society.

From what has been said it may be seen that the reduction of carbohydrates signifies much more than a mere game of hide-and-seek with the glycosuria. Through blind indulgence very material injury may be caused, but through a limitation of the ingestion of

carbohydrates, regulated according to the necessities of the individual case, a very positive advantage may be gained.

d. Significance and Limitations of a Diet of Fat and Albumin.—As we have seen, the proteids and fat must constitute the main portion of the diabetic's diet, and in severe cases the question will arise whether in conjunction with other articles which contain no carbohydrates (certain vegetables, salt, water, alcoholic beverages, tea, and coffee), they shall not constitute the sole diet.

Experience has shown that there is not the least difficulty in a moderate restriction of the carbohydrates, such as is called for in mild cases. Almost every diabetic willingly submits to a permanent exclusion of sugar, sweetmeats, sweet wines, sweet fruits, the cereals, puddings, etc., from his diet if he is allowed a moderate quantity of bread, potatoes, and certain fruits, and is not forced to be always on the lookout to see that a little flour more or less is not used in the preparation of his vegetables and sauces. The loss in nutritive material through exclusion of the saccharine and starchy foods is easily replaced by a somewhat greater ingestion of flesh meat, eggs, fat smoked meats, such as ham, sausages, dried fish, and the like, so that the amount of available fuel corresponds to the daily needs and the patient's strength is maintained. This is the situation of many, indeed most, diabetics.

The difficulties begin when all the carbohydrates ingested, even the smallest amounts, appear again in the urine, or when a greater amount of carbohydrate is excreted than is taken into the system, and when the strictest abstinence does not prevent the occurrence of glycosuria. These are the cases in which over-zealous physicians prescribe an exclusive meat diet, allowing at the most a couple of eggs and a little green salad in addition. With such a diet, however, it is absolutely impossible to introduce enough nutritive values to compensate for the loss of material and of energy in the organism. Even 1,000 grams of meat and six eggs furnish at the most but 1,500 calories; a deficit of 1,000 calories or more remains with its injurious consequences. It is no wonder that patients under this diet excrete very little or no sugar, or that they at the same time grow weak and wretched and succumb finally to heart failure, coma, or any one of the multitudinous complications. Nevertheless the medical adviser has had the mournful satisfaction of seeing the diabetic suffer and die without any sugar in his urine!

Sensible physicians prescribe, therefore, large quantities of fat in addition to the proteids. Even in Germany, where for a long time, contrary to the practice in Latin countries, there was an unaccountable opposition to the ingestion of any large amount of fat, its

utility has gradually come to be recognized by all. The supplementing of a strictly flesh diet with fat marks an essential advance in the therapy of diabetes, for the great importance of fat as a fuel makes it easy to maintain the calorie value of the food to the desired and necessary height. The fear that diabetics would not readily absorb large amounts of fat (150 grams and more) has been shown, except in the rarest instances, to be unfounded. The further fear that the large ingestion of fat, although it might indeed cover the calorie changes, would not suffice, in the absence of carbohydrates, to prevent the breaking-down of the important albumin of the tissues has also been dispelled by the results of Weintraud's beautiful studies in metabolism.

The only objection that remains against a fat-and-meat diet in severe cases of diabetes is the theoretical one that it favors the occurrence of coma. I can only say that in the case of a thing upon which so little calculation can be made as the occurrence of diabetic coma, and in view of the fact that coma has been observed under all forms of diet, we should be very careful how we use the word "favor." Only an extensive critical comparison of statistics, which has never yet been made, could give objective support to this opinion, and put to one side the subjective judgment of the physician theoretically disposed to one or the other view. Single cases prove absolutely nothing here. Furthermore it must be noted that the opposition, which the fear of coma has aroused, to a diet containing no carbohydrates relates properly to a purely flesh diet and not to the improved fat-and-flesh regimen. I have already shown that the former weakens the body and thereby predisposes to coma, but this cannot be asserted of a generous fat-and-flesh diet. From what I have been able to glean from the literature, from what I myself have seen, and from what has been related to me by other judicious partisans of the fat-and-flesh diet (one often learns more of therapeutics by verbal exchange than by the most exhaustive study of the literature), it appears to me that the dread of coma so produced is wholly unfounded. I believe, therefore, that for every really grave case of diabetic glycosuria, the fat-and-flesh diet to the exclusion of carbohydrates is to be regarded as the ideal regimen, against which no serious objection can be raised.

The actual carrying-out of this regimen is another thing. The practical difficulties demand certain concessions which must be granted if one would be certain of the continued trustworthiness and obedience of his patients. It cannot be doubted that a patient in hospital or in a private sanitarium may now and then be nourished for weeks and months without carbohydrates; the strict military discipline of the institution often keeps the bread-hunger of diabetics in check,

even without the confinement which has been advised by some overzealous physicians. But in private practice, except in the case of the occasional strong-willed individual, and such a one is rarely encountered among diabetics, the patient will not obey the command to abstain from carbohydrates. He will always say that he does, but unfortunately diabetes is one of the diseases that ruin character. Just as the victim of morphine is constrained to deceive his physician and himself, so is the sufferer from diabetes.

The tooth of man in civilized regions is not set for meat and fat with no admixture of carbohydrates. The indispensable fat especially becomes repugnant to him when taken continuously for a long time. Just in proportion as it is easy to take large quantities of fat in connection with carbohydrates, is it difficult to ingest them without the latter. The conscientious patient would soon be led through disgust to reduce the amount of fat and thereby be driven on the rocks of an objectionable exclusively meat diet with its dangers of under-nourishment. All the variety which the richest and finest cuisine can offer in the choice and preparation of carbohydrate-free food becomes insufficient in the long run, for the diabetic even more than the healthy person has a genuine longing for carbohydrates —not sugar and sweets, but bread and potatoes. In this respect, it seems to me, there is an essential difference between obesity and diabetes. The corpulent, especially those in the well-to-do classes, submit to a deprivation of carbohydrates, even the most minute quantities, for months at a time without complaint. I know corpulent individuals who year in and year out never take more than about 30 grams of carbohydrates a day and have no longing to increase this amount. But with the diabetic the case is different; he cries for bread. This craving is doubtless inherent in the nature of the disease.

For this reason all sorts of substitutes for bread have been devised (gluten bread, almond bread, etc.), but all of these answer for a short time only, and a disgust for them soon arises. The only one of value is aleuronat bread, not indeed because it is free from carbohydrates, but because, while containing only a comparatively small proportion of the latter, it preserves the genuine bread taste, and because, as I can testify, it is taken readily for months at a time by some, but by no means all, diabetic patients. What therefore is theoretically undesirable is practically urgently demanded. How this demand can be best and least injuriously met will be discussed in the section on the special treatment of the severe forms of diabetes.

c. Considerations concerning Alcohol in Diabetes.—I have already spoken above (*cf.* p. 82) of the influence of alcohol upon glycosuria, the conclusion being reached that moderate amounts do not at any

rate increase the glycosuria. Nevertheless many physicians avoid alcohol. I cannot agree with them in this course.

Alcohol may be useful in various ways in diabetes and may also under certain circumstances be injurious.

(1) Alcohol is very important in the carrying out of the fat-and-flesh diet, which is poor in carbohydrates, for the ingestion of considerable quantities of fat is greatly facilitated if alcohol is allowed at the same time. Even the healthy individual often feels the need after eating very greasy dishes of a swallow of brandy to remove an unpleasant sensation. It is important in the case of the diabetic not to allow these disagreeable sensations to arise after the taking of fatty food, otherwise a disgust for the latter would soon be excited. Therefore the patient should take from the start a small quantity of alcohol with or after fatty food. The form of alcohol best suited to this purpose is cognac, cherry brandy, whiskey, rum, or the like, either clear or with soda water; a good Burgundy is also very useful in such cases.

(2) Alcohol introduces a not insignificant amount of fuel into the body (see p. 87). One gram produces by its oxidation in the organism seven calories, and while the alcohol is being consumed it saves the consumption of some other non-nitrogenous substance, especially fat. When, for example, heat to the value of 100 calories is to be developed, $100 \div 9.3 = 10.75$ gm. fat is needed; the same effect is obtained by the burning of $100 \div 7 = 14.3$ gm. alcohol. In other words, when a man takes 14.3 gm. alcohol he can, without having to fear a deficit in fuel, leave out 10.75 gm. fat from his diet. Since we often have to give the diabetic very large quantities of fat, it is a matter of great importance that we possess in alcohol a means whereby a certain reduction in the allowance of fat can be effected. Of course we can avail ourselves of this means only to a limited extent, for with large quantities of alcohol a far more harmful factor enters into the equation, namely, the poisonous effect of alcohol upon the protoplasm of the cells (von Noorden and Miura[43]). This effect is, however, to be feared only in case of an excessive indulgence. In view of the dangers of larger quantities I would advise that the average limit of 60 grams of alcohol a day be not exceeded, except only in those cases in which through long-continued indulgence in alcohol the body has acquired a certain immunity against its toxic effects.

(3) In the third place alcohol recommends itself as a good nervine, the dose of which can be accurately graduated, and as a powerful heart tonic. Its effects upon the nervous system and heart must indeed be carefully studied in each case, for it is well known that its action varies considerably in individual cases. In the hands of one

who knows how to individualize alcohol is an invaluable nervine and tonic remedy, but it is a two-edged sword in the hands of the routinist and generalizer. It is especially in those cases in which the body has long been accustomed to the use of alcohol that we are unable to dispense with it as a nervine and cardiac tonic. I have seen its withdrawal in such cases followed by very decided injurious effects, such as obstinate insomnia, great irritability, depression of spirits, anxiety, and a feeling of weakness. For this reason I cannot advise the withdrawal of alcohol even where a concomitant obesity and arteriosclerosis would in principle demand its prohibition. The older the individual is the less reason is there that alcohol should be forbidden. But it is very fit and necessary in cases of this kind that the use of all the stronger alcoholic beverages should be prohibited, and only the lightest wines be allowed.

More particular directions as to its employment will be found in the following sections. By way of explanation it may be stated that 100 grams of alcohol, for the most part without admixture of carbohydrates, are contained in—

2,500 c.c.	Pilsener beer (one litre contains 35 gm. carbohydrate, dextrin, and maltose).
1,200 — 1,500 c.c.	White table wine (Moselle, Rheingau, Pfalz, Baden, etc.).
1,100 — 1,300 "	Medium sorts of claret.
1,000 — 1,200 "	Fine red Burgundy.
1,800 — 2,200 "	Well-fermented fruit wine (extra dry).
280 "	Rum.
260 "	Old rye whiskey.
210 "	Whiskey.
200 "	Arrack.
180 "	Cognac.
180 "	Cherry brandy.

General Hygienic Measures.

I have been forced to anticipate in other places much that would properly come under this heading, and would refer the reader for a fuller presentation of the subject especially to the sections on the etiological treatment of neurogenous diabetes and on the employment of the drink-cure. What has been there said will be touched upon here very briefly merely for the sake of completeness, most of our time being given to other topics.

a. Psychic Treatment.—The sufferer from diabetes is as a rule a pessimist; he takes pleasure in brooding over his fate, doubts of the future and thereby loses his enjoyment of the present, and only too often, even while still in possession of his bodily strength, loses all pleasure in his work as well as his energy of will. It is of the great-

est importance to effect an improvement in this condition, and the success of our efforts here will be more gratefully recognized by the patient and his friends than will our reduction of the amount of sugar excreted in the urine. Our aim is to restore the self-reliance of the patient. Most diabetics know that they are incurable, and they will scarcely believe the physician when, in any special instance, he opens up the prospect of complete recovery. Before all we must overcome the patient's belief that, because he is incurable, he is therefore advancing with rapid steps to the grave, and the further belief that every fractional increase of sugar in the urine is hastening this progress. It is a bad sign when a patient begins hypochondriacally to make his spirits and subjective feelings dependent upon the results of the last urinary analysis by the physician or chemist, instead of taking his own strength as a measure of his actual condition.

No general rules can be laid down by which the mental depression and discouragement of the patient can be overcome. Comforting words, procurement of sleep, resumption of occupation or change of the same, in other cases rest, change of surroundings, travel, drink-, bath-, or cold-water-cures, and the like, above all the clear and unmistakable success, demonstrated by the scales, of a suitable diet, these and many more are the factors contributing to the solution of our problem. It is here of the greatest importance to make a correct choice of measures, after a rapid grasp of the patient's individuality, being guided more by the personal bodily and especially mental needs of the patient than by any therapeutic formula.

In contrast to the over-anxious are the too optimistic patients. These are encountered especially among the rich and idle classes in large cities. A scanty excretion of sugar (0.5 to 1.5 per cent. in the total amount of urine for the twenty-four hours) is hardly regarded as a sign of genuine diabetes, but is said to be only the natural and usual result of a hard winter campaign of rich dinners; banker X or neighbor Y had sugar in the urine for a long time and it did him no harm; the harm that the winter has caused will be repaired all right by a course of the waters at Carlsbad in the summer. One often hears remarks of that kind. The physician must actively combat such an optimism, which borders closely on frivolity, for much good may be accomplished in these cases by the institution of a well-ordered and simple mode of life, and much harm may result from neglect of suitable measures.

b. Muscular Exercise.—Credit is due to Zimmer for having forcibly demonstrated the advantage of muscular exercise in diabetes. Among those who have since thoroughly studied the subject may be mentioned particularly Külz, von Mering, and Finkler. It has been

shown that the glycosuria is in many cases diminished as a result of muscular work, but in other cases the opposite effect is produced. It is evident that the amount of muscular labor must be carefully adapted to the patient's capacity. The sufferer from diabetes should never be over-tired, a warning that is based upon many experiences; for example Frerichs calls special attention to the frequent occurrence of fatal cardiac weakness and of diabetic coma after exhausting labor. In cases in which the patient's muscles are still in condition to increase their carbohydrate consumption during work, and are not forced to seize upon the albumin molecule, their exercise short of fatigue can only be of advantage. It is the best protection against loss of bodily strength and of mental energy, and when the sugar-consuming powers are not too far depressed such moderate exercise may well conserve and strengthen them. Indeed, we often see not only an increased tolerance of carbohydrates during the performance of carefully increasing muscular exercises, but may even note a more favorable condition weeks and months later. It is difficult, it is true, to determine exactly how much of the good results observed is due to the muscular exercise and how much should be attributed to the other factors coming at the same time into play (drink- and bath-cures, fresh air, a suitable diet, etc.). A part of the benefit must, however, be laid to the account of the muscular exercise, leaving easily aside the undoubted improvement which this brings about in the circulation, intestinal peristalsis, and self-reliance of the patient.

In mild forms of glycosuria and in cases in which the muscular strength, including that of the heart, is good, the most extensive use of muscular exercise should be made. But the physician must be cautious and conservative in this respect just in proportion to the intensity of the glycosuria, the unfavorable nutritive conditions, the difficulty of replacing the material consumed in work by abundant nourishment, the weakened state of the heart, the rapidity with which fatigue ensues, and the tardiness of recovery therefrom.

I would warn the physician especially against allowing himself to be guided in his prescription of severe exercise by the fact that the patient is corpulent. Only when an abundance of adipose tissue is combined with strength of muscle is such a recommendation justifiable. In all other cases he should proceed with great caution, accustoming the patient by slow steps to increased work.

As regards the kind of exercise, walking and hill-climbing are the most natural and preferable. The exercise is best taken in the morning and followed by a long rest. Horseback-riding is also a favorite form of exercise; it is a passive exercise which is without doubt good for the circulation and especially promotes regularity of the intestinal

functions. However, in regard to corpulent patients, I would say that the belief that riding reduces flesh is entirely wrong; the horse may grow thin, but not the rider. Riding rather favors obesity in that it greatly increases the appetite. Among the sports, any that cause fatigue are to be forbidden, but some when pursued in moderation are to be highly recommended; unquestionably the most healthful is rowing, then come gymnastics, cycling, and open-air games. When the opportunity for these natural exercises is wanting, or when the patient's strength is insufficient—but only under these conditions—passive movements (medico-mechanical gymnastics), and, if necessary, massage may be employed. It is the fashion nowadays to overestimate their value; they fail to increase the patient's self-reliance or to restore tone to his nervous system.

c. Care of the Skin; Bathing.—The care of the skin holds an important place in the treatment of diabetes. Reference has already been made to the evil effects of its neglect (p. 102). When pruritus leads to scratching the danger is especially great, and eczema, acne, or furunculosis may result, or even erysipelas and gangrenous inflammation. These are all preventable affections, preventable by the exercise of cleanliness. Frequent change of underclothing is absolutely necessary. When the patient's instinct of cleanliness is not to be depended upon, the physician must explicitly order regular sponging and at least two tub-baths a week. As regards the temperature of the sponging and of the baths one must be guided by experience in individual cases, for some bear a low temperature well, others ill (see p. 127). In bathing resorts medicinal baths are given, for the sake of the mental effect upon the patient, in the place of ordinary tub baths, but the kind of bath employed is really of little importance. It does no harm if the water holds in solution a little iron, lithium, bromides, iodides, or sulphur, or if an extract of pine-needles or some medicinal mud is added; the advantage is an imaginary one, but still is one that under certain circumstances is not to be despised. For certain nervous patients with feeble resisting powers weak carbonated salt baths are of special benefit. Strong salt water and cold sea-bathing are suitable for but few diabetics. In cases of general pruritus the addition of preparations of tar is distinctly beneficial.

d. Treatment of Constipation.—Many diabetics are perfectly regular in their bowels, a few have a tendency to diarrhœa, and many again are inclined to be constipated. It is important to combat this tendency to constipation, the more so as a very common experience shows that this condition predisposes to diabetic coma. Inaction of the bowels which has lasted for several days is best met, in these cases as in all others, by a suitable dose of castor oil, calomel, com-

pound infusion of senna, or the like. These remedies should, however, be employed only in exceptional cases. The aim of the physician should be not to allow the bowels to be confined for several days at a time. Ordinarily this is effected by regulation of the mode of living, bodily exercise, accustoming one's self to a regular time for defecation, a reduced ingestion of carbohydrates, and an abundant supply of fatty food. As an adjuvant may be recommended an occasional short course of saline, alkaline saline, or alkaline sulphur mineral waters, but when taken at home the efficacy of the latter is soon exhausted. For temporary use (two or three weeks) glycerin lemonade is very beneficial—citric acid 5, glycerin 30, water 1,000; taken in doses of one-half to one litre (one or two pints) a day. For permanent use a mixture of rhubarb powder with bicarbonate of sodium and sulphur, as much as can be taken on the point of a knife each evening, is preferable to any of the older, and certainly to any of the newer, laxative remedies. Rhubarb may be taken in this form for months at a time without any increase in the dose being necessary. Still there are individual idiosyncrasies, and the physician must take note of them; the same proverb applies in the case of the intestine as in that of the palate: *De gustibus non est disputandum.*

e. Travel.—In such an eminently chronic affection as diabetes the patients are naturally very dependent upon their family and the members of their own household. They often chafe under the necessity, and so much the more energetically the more wretched are their circumstances. It is often indeed a matter of the greatest difficulty to treat a diabetic patient properly in his own home. When the pecuniary conditions are unfavorable the question is chiefly one of diet, and this makes at least a temporary change desirable and demands that the patient should enter a hospital. Here they improve greatly under suitable care and diet; but it should be remembered that they ought to be placed in a sunny, well-ventilated ward and kept as far as possible from contact with those suffering from pulmonary tuberculosis. Unfortunately what is gained in hospital is soon lost again at home, in all moderately severe cases. As with the phthisical so with the diabetic; we have to admit that his treatment in the wretched conditions under which he lives is a thankless and desperate task. His prospects of improvement, or at least of remaining for a long period in a tolerable state, are, under otherwise identical bodily conditions, in proportion to the size of his purse. Poor patients, as a rule, wander from the house to the hospital and from the hospital back to the house, until, after a not very long period, they succumb to exhaustion, coma, or some intercurrent disease.

When the patient's circumstances permit of a free choice, the

physician must often energetically oppose his desire to travel about, to go from cure to cure, from spa to spa, to try new places. Otherwise the patient will become a restless, whimsical "crank," a nuisance to all about him. But the medical adviser may profitably recommend a sensible, well-planned change of residence; for example, it is advisable for a diabetic with marked glycosuria to take up his abode permanently in some mild climate.

The patient should be urged to continue his usual occupation as long as possible, although his duties must often be lightened. Once a year, if possible twice, a tolerably long rest from work should be taken, and during this period, according to circumstances, he should undergo a dietetic treatment with abstinence from carbohydrates (see below), take a simple pleasure trip, or visit some health resort. If neither a strict dietetic regimen nor a course of mineral waters is decided upon, the patient should not at any rate visit any of the large cities. A stay in the country, in the hills, or at some mild seaside resort is under all circumstances to be preferred. The more the patient avoids enclosed places and the more the climatic conditions permit of reclining, sitting, and walking about in the open air, the greater will be the benefits of the trip.

There are still many points to be taken into consideration. Travelling about from place to place is to be avoided; a long stay in one locality under the same external conditions is far preferable. In the choice of this locality regard must be had to the fact that the proper nourishment of the patient demands a variety and good quality of food, and quarters where the table is not good are to be avoided. Where no special indications exist by reason of complicating diseases, the choice of a place suitable for the diabetic is a large one. He should always keep away from damp and cold localities, especially from the seashore where the climate is raw, and from forest resorts where there is little sunlight and much moisture; but a warm and sheltered sea-coast is admirably suited to the requirements of all sufferers from diabetes. Even long sea-voyages at a proper time of the year may be readily permitted.

Young and middle-aged patients will derive much benefit from a stay in the mountains. A visit of three or four weeks' duration in some sunny Alpine resort at an elevation of 1,000 to 1,500 metres (3,000 to 5,000 feet) is often of very great service, especially for those who are at the same time neurasthenic and anæmic, but in general for still fairly robust individuals with a mild form of glycosuria. For the elderly and those whose strength is failing, for patients with glycosuria of considerable or great intensity, and for those with a tendency to gout, more moderate altitudes, under 1,000 metres, should

be selected; especially is this advisable when signs of arterial disease or cardiac weakness are present. The only danger of a stay in the mountains is that the patient is tempted to walk too much and to overtax his strength; he should therefore still be kept under medical control. In many cases a stay in the mountains may be taken advantage of to institute a milk-cure—not that milk should be taken to the exclusion of everything else, but that a certain portion of the nutritive necessities should be met by this fluid (see below). This mode of nourishment is well suited to all patients with the milder forms of diabetes, especially young and very old persons. Even when the glycosuria is moderately severe, the milk cure may advantageously be prescribed for a time, for example after a strict fat-and-flesh diet has been maintained for a certain period.

V. Special Treatment of the Individual Forms of the Disease.

After we have studied the general therapeutic methods, their rationale and their bearing, it is necessary to consider the indications for their employment and their mode of application in special cases. This is in general the carrying-out in practice of the principles of diabetic treatment. The guiding factors are the intensity of the glycosuria and the degree of tolerance for carbohydrates. The conscientious physician can dispense with a determination of these factors only in the mildest cases. Of course the consideration must be limited to certain types of diabetes, and it is understood that every case of this protean disease cannot be included in any schema. A special section will be devoted to the treatment of the complications of diabetes.

1. Mild Forms of Glycosuria.

It is common to all the mild forms that the withdrawal of carbohydrates from the food causes a disappearance of sugar from the urine. I shall consider here, however, only those cases in which a certain amount of carbohydrates may be taken without causing glycosuria, while those cases in which a sugar-free urine can be obtained only by complete abstinence from carbohydrates I have placed, for practical reasons, in the class of moderately severe forms of glycosuria.

The determination of the intensity of the glycosuria, according to the method which I have previously described (p. 80), would lead to the formula:

Tolerance = standard diet + x (from 50 to 150 gm.) starch.

On practical grounds I make a distinction between mild forms of glycosuria in elderly patients and those occurring in early life.

a. Mild Glycosuria in Elderly Persons.—It is not necessary to determine with special accuracy the tolerance in persons of somewhat advanced age (say over forty-five or fifty years), usually more or less corpulent or gouty, in whom a small amount of sugar (0.5 to 2 per cent.) is excreted under ordinary conditions, which amount is reduced to a mere trace by a considerable abstraction of carbohydrates from the food. That would be carrying a striving for exactitude to needless lengths.

The form of the glycosuria is benign. The patient is, indeed, not secure from all complications, but the glycosuria will not greatly reduce his strength unless he be maltreated. Unfortunately that often happens. I know of cases of this sort in which a whole pharmacopœia of drugs have been poured into the unfortunate patient, and in which the sufferer has been made so anxious by the saccharophobic physician that he hardly dared to satisfy his hunger, seeing the carbohydrate-ghost in every dish, giving up the use of wine to which he had become accustomed during a long and industrious lifetime, and falling before his time into a hypochondriac and wretched old age—and all that without the slightest necessity. Of course, careless neglect would be just as inexcusable.

The following is the plan of treatment that I would advise:

(1) *Diet.*—It would be to little purpose and would lead to unnecessary anxiety to lay down minute directions as to the choice and quantity of food. It is sufficient to forbid certain articles which consist entirely or in great part of carbohydrates and which experience teaches are often taken in excess, and to reduce the ingestion of certain other articles.

Forbidden: Sugar, sweetmeats, pastry, sweet wines (especially sweet champagne), gruels, dishes made of flour or flour preparations (such as maccaroni and flour puddings), rice, preserves, and sweet jellies.

Permitted in Reduced Amount: Beer, in quantity of not more than one-third to one-half litre (one or two glasses) a day; heavy wines, which, however, had better be replaced by the lighter sorts.

The patient should take his meals at the ordinary times with the family, and may be allowed to eat bread and potatoes according to his desire and take no special account of the proportion of starch contained in the vegetables set before him. On this diet in most cases the quantity of sugar in the urine is insignificant; as a rule the excretion of sugar amounts to from 10 to 20 grams in the twenty-four hours. It is better to put up with such a slight glycosuria than to get rid of it by a rigid exclusion of carbohydrates.

When the quantity of food, under this diet, is left to be regulated

by the patient's appetite there is apt to be a gradual loss of flesh, due to the restriction in the amount of carbohydrates; especially when the muscular exercise is increased above that which the patient has been accustomed to take. Only in the case of the most robust patients should an average loss of weight of about 100 grams a week be exceeded; and in any case the emaciation should not be allowed to proceed very far, for it must be remembered that diabetics feel better and are better protected against danger when their body weight, that is to say their store of fat, is above that desirable for the healthy individual. The older the patient is and the longer the corpulence has existed, the more cautious should the physician be in this respect.

When obesity is not present or when it is desirable to prevent any further loss of fat, the choice as to kind and amount of food should not be left wholly to the patient. It usually answers the purpose to induce him to increase the amount of fatty food in his diet; for example he should always butter his bread and potatoes very freely and should take every day some fat meat (such as bacon and the like), eggs, and some of the more fatty sorts of cheese (see the list of fatty foods at the end of this article). As a rule this general exposition of the significance of fat suffices. When it does not, and the emaciation increases, we must institute the dietary which will be described later as appropriate for cases of mild glycosuria in young persons and for those of the moderately severe forms.

(2) *Drink.*—As drink, in addition to one-half to three-quarters of a litre of light wine, may be taken small quantities (one-third to one-half litre) of beer, and to the morning coffee or tea and the after-dinner coffee may be added some kind of a carbonated table water (Apollinaris, Birresborn, Gerolstein, Harzer Sauerbrunnen, Nieder-Selters, Roisdorf, and the like) or a weak alkaline mineral water, such as the Salzbrunner Kronenquelle, Biliner Sauerbrunnen, etc. The daily amount of these waters may reach one-half to one litre (one or two pints).

(3) *Muscular Exercise.*—Elderly patients should on no account, unless the presence of certain organic diseases furnishes a contra-indication, fail to take bodily exercise. This exercise is to be regulated as to its extent and kind according as it is prescribed more in the interest of general hygiene or with the special object of effecting a certain reduction in flesh.

(4) *Special Cures.*—When the patient's circumstances permit, he should be ordered every year to take a several weeks' course of the waters at Carlsbad or some other place of the same character, or, if he is more delicate and needs rather gentle treatment, at some resort with simple muriatic or alkaline muriatic springs. The latter pos-

sess an undoubted advantage in cases in which the diabetes is engrafted upon a gouty constitution. After the use of the waters for ten days or two weeks we often see in such cases the outbreak of a paroxysm of gout, which is to be regarded as of favorable omen. Drink-cures carried out at home have not the same effect. A severe course of the waters instituted for the purpose of reducing the patient's flesh should be avoided.

For further consideration of the management of this class of cases the reader is referred to the remarks on general hygienic measures in a preceding section.

b. Mild Forms of Glycosuria in Young Persons.—This form of the disease is less frequently associated with obesity or gout, but more commonly follows some morbid change in the nervous system. Indeed it often looks as though the diabetes owed its origin to over-irritation and exhaustion of the nervous system. Therefore the general rules for the management of neurogenous diabetes which have been considered above (p. 126) are applicable to many of the cases falling in this category.

(1) *Diet.*—Whatever the special indications may be in individual cases there is one general rule applicable to all, viz., we must be much more cautious about allowing carbohydrates to young patients with mild glycosuria than to the elderly, and the more so the younger they are, for the reason that the results of carelessness in diet are much more evident and the danger that the glycosuria may assume a progressive character is much more threatening. The diet must be so regulated as to provide for an intake that is sufficient as regards calorie values, while at the same time there is no, or at most a very insignificant, excretion of sugar. In view of the varying intensity of the glycosuria in young persons, it is advisable that an exact determination of the limits of tolerance, according to the formula previously given (p. 80), should be made at least twice a year. For on the one hand it is undesirable to reduce the amount of carbohydrate in the diet of these patients below what is absolutely necessary in order to keep the glycosuria in check, and on the other it is injurious to exceed the tolerance to any appreciable extent.

We can very profitably make use of the easily decomposed carbohydrates (see pp. 81 and 136) in these cases, and preferably of milk sugar which is fortunately combined with other nutritive materials in milk. Often, indeed, formal milk cures are serviceable (see below). The other sorts of sugar are less suitable for this purpose: levulose (fruit sugar) is not good because it cannot easily be taken for any length of time in sufficient amount; cane sugar is not, because if allowed at all it is often consumed in quantities beyond the pre-

scribed limit; furthermore, its withdrawal from the food, to which the patients quite readily become accustomed, opens up the possibility of allowing more bread and potatoes, a matter of much greater importance in the long run. Where the patient cannot accustom himself to do without sweetening in certain dishes and drinks he had better employ saccharin.

The best means of determining the amount of carbohydrate that may be allowed is by the addition of milk to the daily bill of fare. The standard diet (see p. 76) is first increased by the addition of one litre of milk a day, and then it is ascertained how much starch (in the form of bread) can be added to the food without giving rise to glycosuria. If the case is really a "mild" one, the amount of permissible starch ought to be from 60 to 100 grams. The regulations concerning the ingestion of carbohydrates and the general institution of the dietary will vary in different cases. We will first consider the matter of carbohydrates.

In many cases, especially young people who are obliged to eat in restaurants, it is advisable for the sake of simplicity to forbid the use of all articles containing carbohydrate except bread and potatoes; these are sugar, sweetmeats, pastry, sweet stewed fruits, preserves, sweet jellies, thick soups, farinaceous dishes, maccaroni, rice, beans, peas, and the like, and sweet wines. On the other hand, fresh vegetables and fresh fruits in moderate quantities may be allowed. In this respect the dietary is much the same as that prescribed in mild forms of glycosuria occurring in elderly persons. But it differs from the latter in that there must be a limit in the consumption of bread and potatoes, to be determined by the ascertained tolerance and by individual peculiarities, beyond which the patient cannot go; say, on an average, 100 gm. bread and 150 gm. potatoes. The patients soon learn, after having weighed the portions once or twice, to estimate by the eye the amount allowed them.

Other patients are not content with bread in all varieties, potatoes, vegetables and fruit; they want to vary the form of carbohydrate, and especially they long for farinaceous foods and sweets. There is nothing in the way of yielding to this desire, but the patients must be instructed how to order the change; they must be shown how to omit a portion of the bread or potatoes allowed them and to substitute therefor an equivalent from the dishes given in Diet Table III. (see below). This is somewhat circumstantial, and demands a certain amount of intelligence on the part of the patient and careful watchfulness on the part of the family.

The prescriptions thus far have been essentially of a negative nature. But the question of the dietetic management of these cases

is not exhausted in simple negation. This is a point that is often forgotten to the patient's detriment. In view of the restriction as to carbohydrates it is much more important here than in the case of elderly patients to maintain the calorie values of the food. We have to do with individuals who have no fat to consume or at any rate cannot afford to lose much fat, and also with persons in whom the metabolic changes are much more active than they are in the elderly. The reduction of carbohydrates leads only too readily to an involuntary reduction in the ingestion of fat. It is seldom sufficient to rest content with generalizing to the patient concerning the great nutritive significance of fat; the physician must have a certain guarantee that there is a sufficient amount of nourishment, and especially of fat, taken. I therefore make it an iron rule that a certain fixed quantity of fatty food is to be included in the daily dietary. This necessary daily amount may be taken as desired in divided portions with the different meals.

Only in the case of milk, which I always prescribe for this class of patients, do I lay down the definite rule of which experience has often proved the value, that one-half litre (one pint) is to be taken in the morning before rising and another half litre in the evening at bedtime; this amount should not be swallowed at once but rather sipped slowly, at least twenty minutes being taken in its consumption. Many prefer sour milk, kephyr, or kumyss to fresh milk, and there is no objection to it. I consider the drinking of a litre of milk a day of great value in these cases. Patients often say that they cannot take milk, but that is purely imagination; except in the case of those sufferin gfrom certain diseases of the stomach, intestines, or peritoneum, in which diseases a temporary abstinence from all food is demanded, there are almost no people who do not bear milk well or who cannot accustom themselves to its use.

The amount of fat which is to be taken under this "iron rule" varies in the individual cases from 80 to 100 grams. Alcoholic beverages, to the daily amount of at least 30 grams of alcohol, may be added in order to economize in fat. I would recommend the following as the definite quantity of fat-containing foods which must absolutely be taken in the twenty-four hours.

60 gm. butter (with bread, bread and cheese, and potatoes)—480 calories.
2 eggs—150 calories.
10 gm. olive oil (with salad, cucumbers, etc.)—90 calories.
30 gm. fatty cheese—115 calories.
1 litre of milk (fresh or sour)—590 calories.
30 gm. alcohol—210 calories.

This amount of nourishment assures to the organism an energy-equivalent of about 1,600 calories. If the patient, while obeying the above-given directions as to carbohydrates, consults his own taste as to the rest of his food, the amount will always be sufficient, unless there is an extraordinary degree of anorexia, to bring the total value of available food to the required 2,500 calories or more.

As before mentioned the diet in this form of the disease must be so ordered that the excretion of sugar is either *nil* or very insignificant in amount. To obtain this result and at the same time to maintain the nutritive value of the food to the desired height is most difficult in practice in these forms of diabetes—often more difficult, indeed, than in the severer forms. For most of these patients do not feel sick at all; they scarcely credit the physician when he says that they need a special diet; they are greatly inclined to excesses in eating and drinking, and are often prevented by their social position and their calling, as well as their desire for companionship at home and elsewhere, from giving the necessary attention to their diet as regards quantity and quality. It is often a difficult task for the physician to keep the patient's will-power firm and to hold him in the middle path as far removed from careless neglect of necessary precautions as from discouragement and hypochondriasis.

b. General Directions.—As regards the management of the case in other respects enough has already been said in the appropriate sections (especially in that on Neurogenous Diabetes, pp. 126 and 142). But I desire to give prominence to the following points meeting the special indications present in the cases under consideration:

Care that there shall be regular mental employment as well as regular muscular exercise (as regards the use of the latter for increasing the tolerance for carbohydrates, see p. 143). Caution against excess in both these directions.

Caution against excess in the use of alcohol, tobacco, tea, and coffee.

As regards mineral-water cures, the alkaline muriatic waters frequently answer better than those containing sulphur. The first are to be avoided in proportion as nervous irritability and a neurasthenic condition form a prominent feature in the morbid picture. Although the alkaline muriatic springs are not so distinctly prejudicial to patients of this kind as are the waters of Carlsbad, Marienbad, and the like, still the sufferers are often much more markedly benefited by being sent for the warm summer months to some subalpine resort with an elevation of 800 to 1600 metres (2,500 to 5,000 feet). The stay in such a resort may be taken advantage of by patients with a slight degree of glycosuria for the institution of a milk-cure. Experience

has shown that milk is taken in large quantities much more readily in the mountains than at home. Three litres of milk may without difficulty be added each day to the diet with no fear that not enough other food will be taken. During the milk-cure the patient should avoid all starchy and saccharine food, including bread and potatoes, and eat only so much farinaceous matter as may be needed in the preparation of the meats and vegetables to make them palatable. Three litres of milk yield about 1,800 calories; 40 grams of alcohol, which is best taken in the form of cognac, cherry brandy, or the like, added to the milk or drunk after it, yield 280 calories more. With a normal appetite, which is seldom wanting in the mountains, the meat, fish, eggs, well-buttered vegetables, etc., easily bring the total calorie value of the food up to 3,000 or more. The three litres of milk contain about 135 gm. milk sugar. In mild forms of glycosuria, which we are now considering, there will be no sugar, or at most only 15 or 20 grams a day, excreted in the urine during the continuance of the "cure." Even when in the first few days of the treatment a somewhat larger amount is excreted, it is not necessary to discontinue the cure, for the glycosuria almost invariably sinks in a short time, a result to which the favorable hygienic conditions and the mountain air doubtless contribute not a little. Should the glycosuria not diminish, the milk sugar evidently exerting an unfavorable influence upon it, we may still resort to kephyr, which is comparatively poor in milk sugar, a part of which (from one-third to one-half of the entire amount) is destroyed in the process of alcoholic fermentation. Kephyr should not, however, be recommended except in those cases in which experience proves that milk is injurious. The organ of taste does not recommend kephyr to civilized people as a permanent beverage; it is a drink that cannot hide its barbaric origin.

2. Moderately Severe Forms of Glycosuria.

Under this heading are classed the cases in which the excretion of sugar is arrested or reduced to small amounts (from 10 to 20 grams) only by total abstinence from carbohydrates, that is to say, in which but an insignificant amount of carbohydrates can be borne. Any increase in the quantity of these substances will excite such a degree of glycosuria that the available value (the difference between the amount of carbohydrate of the food and that of the sugar in the urine) is very minute. The limit of tolerance varies also in these cases, but unfortunately the variation is more often in the direction of a decrease than in that of an increase; this is especially the case in young persons, for the moderately severe and severe forms of diabetes in childhood and early life give no quarter.

This form occurs usually in the young and middle-aged, seldom in those of later years. An hereditary influence is frequently evident, and there seems often to be a neuropathic basis for the disease; a gouty diathesis is more rarely present; obesity is uncommon, emaciation frequent.

In prescribing a suitable diet it must be remembered that the carbohydrates are not to be counted on as a nutritive material, although they cannot be permanently excluded as an accessory food, and that the calorie values lost by the abstraction of carbohydrates must be made up by an increased supply of fat and albumin.

The limits of tolerance must be determined at the beginning of the treatment and frequently thereafter at intervals of several months. If this is not done a slight tendency to improvement or deterioration may be overlooked and thus no advantage be taken of it to institute the necessary changes in diet.

I would recommend that *these patients be subjected to a three-weeks' course of complete abstinence from carbodydrates at least twice, and if possible three times, in the year, while in the intervals a certain amount of carbohydrates may be allowed.*

We may take this opportunity to state, however, that there is actually no absolute carbohydrate-free food that man can eat. Even meat, eggs, and the lightest kinds of vegetables always contain minute quantities, and under the most carefully ordered diet at least 10 to 20 grams of carbohydrate will be taken in the day.

The intercalation of these periods of a strictly regulated diet has the advantage that it reminds the patient of the need of great watchfulness over his food and constantly renews, as it were, his moral support; it has the advantage that these periods can be employed to determine the oscillations of tolerance; and, above all, it has the advantage that during these periods opportunity is given for a strengthening of the sugar-consuming function so that it may be better prepared to deal with new accessions of carbohydrates (*cf.* page 130). Every diabetic also, whose will-power is even half-way preserved and who earnestly desires the improvement, or at least the maintenance, of his strength and the prolongation of his life, is ready and willing to undergo a course of strict dieting of such short duration; and the more so as by these short periods of deprivation he gains the permission to indulge again during the longer intervals in his wished-for carbohydrates.

a. The Diet in the Periods of Strict Abstinence.—The difficulty consists in providing for the necessary amount of fat without the foundation of carbohydrates. There is no lack of tasty dishes for an albuminous diet. The distribution of the nourishment through

five meals is very necessary, otherwise the required amount will not be taken. As there must be the greatest variety from day to day and individual tastes must be most carefully catered to, it is impossible to lay down any satisfactory special directions applicable to all cases. The physician must consult with the patient and pay attention to his special preference and antipathies. The patient will derive no assistance from short general rules laid down during his visit in the physician's office; they only confuse and discourage him. The dietetic treatment of such an individual demands the sacrifice of time, patience, and thought. But it is only in the beginning, during the preliminary consultations, that the patient should be allowed to give expression to his wishes as to the daily bill-of-fare; this responsibility should then be taken from him, for it would only annoy and worry him and might readily excite a disgust for many articles of food. As it is only in rare cases that the domestic kitchen will suffice for the needs of the patient and of the physician, it is advisable that, while following out the strict dietary course, the patient enter a hospital or some private institution under the physician's direct control, at least for the first course. During this period the physician must give a definite prescription for the diet, as to both quality and quantity, from day to day. The patients themselves will learn how they should live during the subsequent courses. The educational side of such a course of treatment in an institution and under the direct supervision of the physician is not sufficiently appreciated. It is as beneficial to the diabetic—*mutatis mutandis*—as to the sufferer from gastric troubles, pulmonary phthisis, neurasthenia, etc.

When I present the following bill-of-fare, I do not contradict what has just been said as to the impossibility of its general application. It is given only as a sample of the diet for *one* day in a special case. Whoever would undertake the direction of such a course of treatment must study special works dealing with the composition of nutritive materials, must make special culinary studies, and, as far as lies in his power, undertake investigations himself in the line of food preparation. In the way of explanation I would refer the reader to Diet Tables I. and IV., given below. The dishes there given and other similar ones must serve as the main reliance in providing for the nourishment of the patient. Only in case of necessity may some of the dishes given in Table II. be made use of. In general the "cure" is the more easily carried out, the fewer are the concessions made; once a point is yielded there is no end to the argument and to entreaties for permission to indulge in one or the other special dish.

It is strongly to be recommended that the physician who would assure the success of a strict dietetic course should himself try living

for a time under the same regimen. He will thereby learn much which he can later apply to the advantage of his patient.

A Sample Bill of Fare.

The aim is to provide nourishment to the value of 2,500 calories, with the least possible ingestion of carbohydrates.

		Albumin. gms.	Fat. gms.	Alcohol. gms.	Calorie values.
8 o'clock, first breakfast.	100 gm. ham	25	36	..	497
	1 cup of tea	..	..	..	
	1 glass of cognac	..	..	8.5	
10 : 30 o'clock, second breakfast.	2 eggs	14	11	..	234
	fried in 10 gm. butter	..	8	..	
12 : 30 o'clock, luncheon.	150 gm. cold roast meat	57	8	..	912
	Mayonnaise made with the yolk of one egg and one spoonful of oil.	3	18	..	
	Raw cucumber, with 5 gm. vinegar, one spoonful of oil, salt and pepper	..	15	..	
	15 gm. Gorgonzola cheese	4	5	..	
	Half-bottle of Moselle	..	..	25	
	1 cup of coffee, with one tablespoonful of cream	..	5	..	
5 o'clock, tea.	1 cup of tea	..	..	..	144
	1 boiled egg	7	6	..	
	1 glass cognac	..	..	8.5	
7 : 30 o'clock, dinner.	1 cup of bouillon, with 15 gm. marrow	..	14	..	1,074
	80 gm. boiled salmon	18	11	..	
	⅛ to ¼ lb. asparagus, with 20 gm. butter	..	16	..	
	30 gm. smoked ox-tongue	8	6	..	
	100 gm. capon	17	12	..	
	Salad, with 5 gm. vinegar and one spoonful of oil	..	15	..	
	Half-bottle of Burgundy	..	..	30	
10 o'clock, night-cap.	1 glass of cognac with seltzer-water	..	..	8.5	59

This amount of nourishment for the day, containing about 150 gm. albumin, 185 gm. fat, and 80 gm. alcohol, represents in round numbers the very considerable value of 2,900 calories. It therefore makes allowance for the possibility that all the dishes will not be taken in the prescribed quantity. If we omit the alcohol there will still remain a nutritive value of about 2,375 calories. As to the rules for computing the calorie values, see page 87.

During the strict dietary course the patient had better lead a quiet life, avoiding society and any intellectual strain or exciting reading, and limiting his bodily exercise to a walk of an hour or an hour and a half duration. It is advisable also that he should be in the open air as much as possible, sitting on the veranda, taking his daily

exercise in the garden, and sleeping with open windows. The use of Carlsbad or other similar mineral waters is to be discontinued. As a drink or to dilute the wine any indifferent carbonated water may be taken in desired amount. Any strict bath treatment is to be avoided. A warm bath twice a week and daily spongings with moderately cold water are advisable.

b. The Diet in the Intervals.—At the end of this period of "strict diet" bread should be given in gradually increasing quantities to determine whether the patient's limit of tolerance is essentially raised. If the tolerance is much greater (which it seldom is), carbohydrates may be given with a freer hand and a dietary established somewhat after the regulations applicable to the milder forms of glycosuria in young people. Ordinarily more restrictions are called for than in those cases, and these are to be effected in the following way:

It is immaterial whether glycosuria returns or not under this diet or how intense it is, at least as much carbohydrate is to be allowed in the day, in addition to the traces always present in meat and green vegetables, as is contained in 120 grams (4 ounces) of good wheat bread (66 gm. carbohydrate). This is the average amount permissible in most cases; only exceptionally, when careful observation for several days shows that glycosuria is absent or that less than 10 gm. sugar is excreted in the twenty-four hours, may as much as 150 grams of wheat bread be allowed. In order to assure an average calorie value of 2,500 (see p. 134) the ingestion of a certain quantity of fat must be absolutely insisted upon (p. 153). As in these cases, in distinction to the milder forms, milk is not included in the fixed dietary rule (see the section on Milk-cure, below), and as the body derives little benefit from carbohydrate as a food, the fat must be prescribed in greater quantity and under another form. There is no great difficulty in providing a suitable quantity of fat in palatable form, if the physician will devote a little thought to the matter and if the patient can have his food specially prepared. Of course special directions must be given as to what dishes are allowable and what not, and in what amounts flour, sugar, starchy vegetables, etc., are to be permitted (see below). If under these favorable circumstances the rule is adhered to that every dish must contain as much fat as it can, and yet be palatable, in the form of butter, cream, bacon, olive oil, yolk of egg, marrow, etc., the patient will receive in this way from 120 to 150 grams of fat, having a value of from 1,100 to 1,400 calories, a day. In addition there is the butter which he puts on his bread and potatoes, amounting to at least 40 grams a day, and containing 35 grams of fat with a calorie value of 325. If the diabetic is further directed to drink at least a pint of light or moderately heavy wine and to take

a small glass of cognac or old whiskey after any especially fatty food, he will easily reach an amount of 40 grams of alcohol a day, representing a further value of 280 calories. In this way we are assured of the daily ingestion of food to the value of 1,700 to 2,000 calories. The necessary remainder will be furnished by the proteids and in a small measure also by the carbohydrates.

The difficulty is greater if the food cannot be specially prepared for the diabetic. The dishes then come to the table prepared with much less fat, and we must take greater pains to see that the "iron rule" as to fat is adhered to. I would recommend the following prescription concerning the addition of fatty substances to the diet, it being of course understood that they are subject to alteration as to quantity and quality in order to provide for variety and to meet individual indications:

Butter: 100 grams (3 ounces) of butter (containing 85 grams of fat having a value of 890 calories) must be weighed out every morning for consumption through the day. The patient eats it as he will on bread, potatoes, vegetables, meat, fish, etc., either in solid form or melted, according to the nature of the food with which it is to be taken.

Olive Oil: 20 grams, a tablespoonful (with a value of 186 calories), should be taken on salad (lettuce, chicory, cress, cucumber, tomato, red cabbage, etc.). With that used in the preparation of mayonnaise dressing for salad, cold meat, fish, lobster, etc., the total amount will easily reach 40 or 50 grams in the day. In that case it may be possible to omit a portion of the butter or bacon.

Bacon: 20 grams (containing 15 grams of fat with a value of 140 calories) of either smoked or salt bacon, should be used in frying eggs, in the cooking of omelets, or in the preparation of various meat and vegetable dishes.

Eggs: 5 eggs are to be taken prepared in various ways; five medium-sized hen's eggs contain about 35 grams albumin and 27 grams fat, and have therefore a value of 390 calories.

Alcohol: About 40 grams (an equivalent of 4 tablespoonfuls of brandy a day) under various forms, with a value of 280 calories.

By means of these articles the body will receive nutriment to the value of about 1,900 calories, of which more than 1,600 calories will be yielded by the fat. The ingestion of these considerable quantities of fat may, as I have often convinced myself, be easily effected, and is not seriously contended against by either women or men who appreciate the necessities of their disease and are inclined to yield to them.

Up to the present we have considered only the permissible quantity of bread, as being the chief and most important representative of carbohydrate foods, and the amount of absolutely necessary fat that

is to be taken. The other articles of diet may be grouped under the following headings, easily comprehensible by the diabetic and by those who have to prepare his food:

(1) *Unconditionally Allowable Foods.*—These are free from carbohydrates or contain them only in very minute quantities. See Table I., below.

(2) *Foods Permissible in Moderate Quantities.*—These contain carbohydrate, but so little in proportion to the mass of the food that it need not be taken into account and calls for no compensation by limiting the amount of bread permitted. Some of the foods in this group are proportionally richer in carbohydrates, but the absolute amount in which they are ingested is small. Examples of dishes in this category are given in Table II. Three or four of these articles, in the amounts given in the table, are to be selected for the patient each day, but the physician must use his own judgment in individual cases as to whether to allow a larger amount of each dish or a greater number of dishes either temporarily or permanently.

(3) *Conditionally Allowable Foods.*—These for the most part contain a large proportion of carbohydrates. They should be taken in measured quantities, compensation being secured by reducing the usual allowance of bread. The relative value of these dishes, as compared with bread, is given in Table III.

(4) *Especially Valuable Foods.*—These are serviceable because of their large proportion of albumin and fat and their correspondingly high calorie value. Some of them contain small amounts of carbohydrates. A list of them will be found in Table IV.

The dietetic rules just given are undoubtedly applicable for the most part to the longer intervals between the periods of strict diet. Both patient and cook soon learn from them to pay attention to the quality as well as the quantity of food. The patient should naturally have as little as possible to do with the weighing and measuring of his food, and for this the cook must be made responsible. This can easily be done in every well-regulated household, although it demands increased work and presupposes the exercise of loving watchfulness. It will also be necessary, in all but the mildest cases of glycosuria, to prepare certain dishes expressly for the patient.

The question of a milk diet demands a few words. From the data given in Table III. it follows that, if desired, a portion of the allowance of bread may be replaced by milk,—for example, a litre of milk may be substituted for 50 grams of bread. Many patients are glad of this permission and avail themselves of it for long periods or permanently. But to the majority the remaining allowance of bread seems too small, especially when the gratification of a desire for va-

riety demands a further curtailment of the permissible quantity. These difficulties may be considerably lessened if the patient is content to use aleuronat bread, which contains much less starch. The allowance of carbohydrates may then be apportioned as follows:

1 litre of milk, equivalent to 50 grams of bread.

100 grams of aleuronat bread, equivalent to 50 grams of bread.

Other dishes selected from Table III., as for example:

90 grams of new potatoes, equivalent to 25 grams of bread; giving a total amount equivalent to 125 grams of bread.

At other times it may be advisable to give the total amount of permissible carbohydrates in the form of milk; for example, instead of 150 grams of bread the patient may drink three litres of milk a day, in which case the dishes from Tables I., II., and IV. only are to be allowed. Those "milk-cures" to which we have referred before in considering the treatment of the mild forms of glycosuria in young persons, are especially to be recommended in greatly weakened individuals and those suffering from grave complications. They should not be continued in general longer than three or four weeks at a time, and are best instituted during the patient's stay in the country or in the mountains.

General Considerations.—As regards the management of the case in other respects, the general rules laid down in a previous section (p. 142) are to be followed. It is to be remarked especially that these patients, even more than those suffering from mild forms of glycosuria, are to be guarded against energetic "cures" and overtaxing of the bodily or mental strength. Long rests and freedom from business cares are to be taken several times a year. A moderate course of some alkaline sulphur water (Carlsbad) is often of great advantage and is best taken after a course of strict dieting. It has already been said that it is better to discontinue the use of mineral waters of this sort during such a course. For other considerations applicable to this class of cases see page 154.

3. Severe Forms of Glycosuria.

Under this heading are grouped those cases in which, in spite of a continued diet as free as possible from carbohydrates, sugar is constantly excreted in the urine. In order to stop the glycosuria entirely the proteids must be restricted as well as the carbohydrates, or even a complete fast may be necessary. These cases are met with usually in early life and are seldom seen after the fortieth year. There is ordinarily emaciation as well as bodily and mental sluggishness. Complications are frequent, and the course of the disease, even under the best therapeutic management, is steadily toward a fatal issue at

the end of a few months or years. Careful dietetic treatment, however, in conjunction with other appropriate measures may undoubtedly, in a large number of cases, retard the progress of the disease, prevent many a complication, and delay the fatal issue for months or years.

As regards the dietetic treatment, the same rules are to be followed in principle as in the management of the cases just considered. Here also, and in still greater degree, carbohydrates are little more than waste material as regards nutrition (see p. 135), they aggravate the diabetic disturbance (p. 137), and yet cannot be permanently dispensed with (p. 140). They are always to be regarded as incidental articles of diet or, as it were, luxuries.

It is advisable, a careful watch being kept on the fluctuations of toleration, to order the diet after the following plan: *At least three times in the year, if possible quarterly, the patient must be subjected to a course of strict dietary treatment.*

a. The Period of Strict Diet.—This differs from the similar course recommended in the treatment of cases falling in the preceding category in that (1) its duration should be four weeks instead of three, and (2) there must be much more strictness in the choice of food allowed. Only in cases of the greatest necessity should one or two of the dishes given in Table II. be conceded, and as a rule the choice should be made from the lists in Tables I. and IV. As regards the educational, technical, and culinary aspects of the course the reader is referred to the remarks on page 157.

During the period of strict diet the drinking of mineral waters is to be discontinued; the patients had better enter a hospital or private institution, give up while there all mental and bodily work, sit in the open air as much as possible, take short walks of fifteen minutes' duration, and occasional drives.

b. The Diet in the Intervals.—During this time carbohydrates in restricted quantities are to be allowed. When we have no reason to fear disobedience or deceit on the part of the patient, we must, despite all theoretical opposition, permit the use of carbohydrates to almost as great an extent as in the case of the patients in the preceding category who are suffering from the moderately severe forms of glycosuria.

The diet will therefore be composed from: Table I., in any desired, but always in large, amount; Table II., three or four articles in the quantity there prescribed; Table III., in amounts equivalent in value to from 80 to 120 grams of white bread. The less of these we can get along with, the better. It is well to vary the amount of food of this kind, giving now more, now less. As regards the use of milk, what

was said in speaking of the moderately severe forms of glycosuria holds equally good here.

In order to assure the necessary consumption of fat we must establish here also an "iron rule" as to the daily amount, taking the table given on page 160 as a basis and making whatever alterations may seem to be indicated in special cases. It is even more necessary here to devote especial thought to the best means of maintaining permanently the ingestion of fat at the desired figure, for fat is for these patients the only thing upon which they can rely to maintain their strength and prolong their lives.

It is also advisable to give these patients a larger amount of alcohol than we should prescribe in the case of mild forms of glycosuria. We may go as high as 80 grams of alcohol a day, such a dose being justified by the greater ingestion of fat, the tendency to heart failure, and the general nervous exhaustion. Naturally the alcoholic beverages which contain no sugar are to be selected. Their percentage of alcohol is given in the table on page 142. I prefer to distribute the total amount of alcohol through the day as follows:

With the luncheon, one pint of Moselle (containing about 25 gm. alcohol).

With the dinner, one pint of good old Burgundy (30 to 35 gm. alcohol).

Three or four times a day, a liqueur-glass of brandy or whiskey with carbonated water or tea (containing in all from 20 to 30 gm. alcohol).

These patients need to be protected in every possible way. Muscular exercise may and indeed should be carried to a greater extent during the intervals of strict dietary treatment, but caution in this respect is always necessary. Any occupation which calls for exhaustive bodily or mental labor should be given up or at least be essentially lightened.

Warm baths of fifteen minutes' duration two or three times a week are very useful; they should always be immediately followed by rest in bed.

Once or twice a year, after the period of strict diet, the patients should take a course of alkaline sulphur waters, or, when exhaustion is pronounced, of alkaline muriatic waters. But we must not look for very great results from such a course in these cases.

VI. Treatment of Complications.

1. *General Rules.*—The complications are in general to be treated according to the indications which they themselves offer; this is

especially true as regards surgical intervention. Still it is to be remembered that many complications resulting from the poor nutritive conditions are most successfully met by the hygienic and dietetic treatment of the glycosuria. I have dwelt upon this fact repeatedly in previous chapters. In general, therefore, the complications call for no change in the rules laid down in the preceding sections, except in so far as they demand a more careful and strict carrying out of the same. The frequent occurrence of complications, dependent for their origin upon the primary disease, will lead us according to circumstances to institute, even in the mild forms of glycosuria, the general line of treatment suitable for the medium or severe forms. A more strict therapy is called for especially in those cases in which obstinate furunculosis, which does not yield to the most painful cleanliness and the most careful local treatment, badly healing wounds, disturbances of vision, neuralgia and inflammation of the peripheral nerves, a tendency to gangrene, etc., are present.

The success attending these measures often puts in the shade all the results obtained by drugs, electricity, massage, and the like. While we follow the general dietary rules—restriction of carbohydrates and increase in the quantity of fat, proteids, and alcohol—in combating the complications, we do so partly on purely empirical grounds. The improvement in the nutritive conditions certainly contributes to the success of these measures, and perhaps also the reduction of hyperglycæmia may have something to do with it; but this is purely hypothetical.

The treatment of many complications has been already briefly but sufficiently considered. In some places I subjoined the therapeutic remarks to the description of the diseases themselves. See especially the sections on complicating affections of the skin and mouth. A few points require particular mention.

2. *Gastro-intestinal Catarrh.*—This is a very grave occurrence and one that is full of danger to every sufferer from diabetes (see page 105). To arrest its progress as speedily as possible it is advisable to prescribe a fast for a day or two at the very beginning, a measure which experience has shown to be productive of the best therapeutic results in this form of disease. But as diabetics, who are at the same time emaciated, have very weak powers of resistance and are exposed to the danger of exhaustion through fasting, we must resort at the same time to very energetic stimulation—red wine, which contains tannin, in doses of $1\frac{1}{2}$ to $2\frac{1}{2}$ pints a day, diluted with boiled water to control the thirst, gives the best results in these cases. A cautious use of opium may also be made. The opposite mode of treatment with purgative doses of calomel, given with a view to intestinal dis-

infection, is less certain in its results, very weakening, and should be instituted only in the case of robust individuals. In debilitated patients it rather provokes what it is our object to prevent, namely, collapse and coma.

3. *Operative Measures.*—As far as possible operations should be avoided, for wounds heal badly and readily become a starting-point for widespreading gangrene. I would especially emphasize the application of this rule in the treatment of boils in diabetic patients. A Nestor of German surgery said recently that he regarded it as an especially difficult task to restrain impetuous surgeons from the operative treatment of boils. If the knife had better be laid aside in the treatment of boils in general, it certainly should be when they occur in the course of diabetes. Furuncles disappear rapidly as a rule upon the institution of a suitable diet, combined with the local application of compresses wet with a mild antiseptic (boracic acid) solution. Of course this warning should not prevent our resort to the knife in the case of deeper-seated inflammations, such as carbuncles and phlegmons following boils.

The fear of an operation is the more justifiable the weaker the patient is and the more pronounced are other trophic disturbances. Besides the local dangers connected with the operation wound, the narcosis itself is to be feared. In any case chloroform should not be employed as the anæsthetic, since it endangers the integrity of the heart, the resisting powers of which are already greatly depressed in diabetes. It is better to use ether with the previous administration of morphine. Besides the accidents liable to occur during the narcosis, there seems to be not infrequently a special tendency to coma excited by the anæsthetic (Becker [44]).

In tolerably severe cases the surgeon should not immediately proceed with an operation which may be indicated, but should rather, where possible, postpone it until after a two weeks' course of a strict fat-and-flesh diet.

4. *Pulmonary Phthisis.*—This complication should not cause any relaxation in the carrying out of the suitable dietetic principles, but rather demands greater strictness and especially the greatest possible increase in the amount of fatty food with the addition of considerable quantities of alcohol. It is advisable that the patients should reside in places where the climate is mild rather than in those lying at high elevations where the air is raw, and treatment in a sanitarium is preferable to a stay in one's own home or in an hotel. Certain hydrotherapeutic measures of a mild character may be cautiously instituted; diabetics with phthisis are individuals demanding the greatest protection against injurious influences. The use of creosote

and guaiacol is to be recommended, but tuberculin seems to me, from the results of observations made three years ago, to be of very doubtful advisability in cases of diabetes. In general the results of treatment of pulmonary tuberculosis in diabetics are very unsatisfactory. And this offers a still stronger reason for care on the part of the physician in guarding his patient against infection with tubercle bacilli, on the one hand by removing him from an infected neighborhood and on the other by maintaining the general nutrition at the highest possible point.

Diabetic Coma.—In many cases there is a prodromic period indicating the approach of coma; this time is to be employed in taking prophylactic measures which seem often to be successful.

a. The form of nourishment must be varied in different ways according to the nature of the case. If the threatened patient has been taking carbohydrates in considerable quantity, they must be greatly reduced and replaced by added amounts of proteids and fat. On the other hand, if the patient has been abstaining strictly from carbohydrates it will be advisable to permit their use. The mere fact of a change seems to be more important than the direction in which this change is made.

b. Large amounts of alcohol, given in divided doses through the day, are necessary.

c. Constipation must be relieved by mild laxatives, but the use of drastic purgatives is to be condemned.

d. Acting upon a theory, which is doubtful yet worthy of attention (acid-intoxication—see p. 95), large doses of alkalies have been recommended; for example, 6 or 8 grams of bicarbonate of sodium a day added to one or two bottles of Vichy or Neuenahr water.

In the actual presence of true coma we are very helpless. Intravenous injections of alkalies, recommended on theoretical grounds, have been found practically to be of no value. I once saw a most surprising result from the recently recommended intravenous injection of a litre of a 0.6 per cent. salt solution, in divided doses of 250 grams given at intervals of four hours. The diminished urinary secretion increased remarkably, and consciousness returned—though only temporarily. I would recommend a further trial of this procedure, which is certainly rational, having the effect of promoting diuresis and washing out of the system any toxic substances which may be present. After this, injections of camphor and ether give most promise; they are at least indicated by one symptom, which is seldom absent in diabetic coma, namely, weakness of the heart.

Diet Tables.

Concerning the use to be made of these tables enough has been said in the preceding sections (see especially p. 161). We have there seen for what cases and with what object the division of the articles of diet into special groups is necessary. The reader will of course understand that the expressions "allowable," "conditionally allowable," etc., are only relative, and that articles which are "conditionally allowable" in the case of one patient may fall into the division of "unconditionally allowable" in that of another.

Table I.

First Group: Unconditionally Allowable Foods.

Fresh meat: All the muscular parts of the ox, calf, sheep, pig, horse, deer, wild and domestic birds—roast or boiled, warm or cold, in their own gravy or with mayonnaise sauce.

Internal parts of animals: Tongue, heart, brain, sweetbreads, kidneys, marrow-bones—served with non-farinaceous sauces.

Preserved meats: Dried or smoked meat, smoked or salt tongue, ham, smoked breast of goose, American canned meats, Australian corned beef.

Fresh fish: All kinds of fresh fish, boiled or broiled, prepared without bread-crusts or cracker-meal, and served with any kind of non-farinaceous sauce, preferably melted butter.

Preserved fish: Dried fish, salt or smoked fish such as codfish, haddock, herring, mackerel, flounders, salmon, sardellen, sprats, eels, lampreys, etc.; tinned fish, such as sardines in oil, anchovies, etc.

Fish derivatives: Caviar, cod-liver oil.

Shell-fish: Oysters, mussels, and other bivalves, lobster, crayfish, crabs, shrimps, turtle.

Meat extracts: Meat peptones of all kinds.

Eggs, raw or cooked in any way, but without any admixture of flour.

Fats of all kinds, animal or vegetable.

Fresh vegetables: Green lettuce, endives, cress, spinach, cucumbers, onions, leeks, asparagus, cauliflower, red and white cabbage, sorrel, French beans. The vegetables, as far as they are suited to this mode of preparation, are best cooked with meat broth or a solution of Liebig's extract and salt, and covered plentifully with butter, lard, suet, or goose fat. The addition of flour is not permissible.

Preserved vegetables: Tinned asparagus, French beans, pickled cucumbers, in brine or vinegar, mixed pickles, sauerkraut, olives.

Spices: Salt, white or black pepper, Cayenne pepper, curry, cinnamon, cloves, nutmeg, English mustard, saffron, aniseseed, caraway-seed, parsley, dill, borage, pimpernel, laurel, capers, chives, garlic, etc. Many of these spices contain, indeed, a rather large percentage of carbohydrates, but they are added to the food in such small quantities that this may be disregarded.

Soups: Clear soups and broths, with or without eggs, marrow, fresh or dried vegetables (Julienne), clear turtle soup, etc.

Cheese: Stracchino, Neufchâtel, old Camembert, Gorgonzola, and all other fatty or so-called cream cheeses.

Beverages: All kinds of natural or artificial carbonated waters, either clear or with lemon juice and saccharin or glycerin, or with rum, cognac, whiskey, arrack, cherry brandy, plum brandy, Nordhäuser rye whiskey, etc. Light Moselle or Rhine wines, claret, or Burgundy in amounts prescribed by the physician. Coffee, black or with cream, without sugar but sweetened with saccharin if desired. Tea, clear or with cream or rum.

Table II.

Second Group: Foods Permissible in Moderate Quantities.

These contain carbohydrates, but so little that they need not be considered, and demand no compensation by a reduction in the allowance of bread. Some of the articles contain a rather large percentage of carbohydrates, but the absolute quantity in which they are consumed is small.

The amounts here given have been fixed by practical experience, and it will seldom be found necessary to increase them. Of the dishes here given, when they are allowed at all, only a few (from two to four) are to be selected each day. It is possible in this way to secure a great variety in the patient's dietary.

Internal parts of animals: Calves' liver, giblets, up to 100 grams.

Sausages: Liver sausages, preferably the fatter kinds, liver sausage with truffles, black pudding, 60 grams. Meat sausages, 80 grams. German sausages, Frankfurter sausages, and the like, brawn, head-cheese, sausage-meat balls, 100 grams.

Patties: Paté de foi gras, potted beef, ham, tongue, salmon, lobster, anchovies, etc., one-half to one tablespoonful.

English sauces, such as Worcestershire, Harvey, beefsteak, anchovy, lobster, shrimp, India soy, China soy, one teaspoonful.

Cream, from four to six tablespoonfuls a day.

Cacao, prepared without sugar, 25 grams.

Cheese: Emmenthal, Romadur, 60 grams; Gervais, Stilton, Brie, Holland, Gruyère, 50 grams; Edam, Cheddar, Gloucester, Roquefort, Parmesan, 30 grams; Cheshire, 25 grams.

Vegetables (prepared without flour or sugar): 5 Teltower turnips; salsify, turnip-rooted celery, turnip cabbage, pumpkin, 2 tablespoonfuls; green peas, beans, carrots, Brussels sprouts, 1 tablespoonful; 1½ artichoke; 1 truffle; 5 medium-sized champignons; 1 tablespoonful of morels or other edible mushrooms.

Raw vegetables: 8 radishes; 2 sticks of celery; 2 medium-sized tomatoes.

Nuts: 2 walnuts; 6 hazelnuts; 3 almonds; a thin slice of cocoanut; 8 Brazil nuts.

Fresh fruits: One thin slice of melon; one small tart apple; one or one and a half peach; one spoonful of raspberries or strawberries; 4 spoonfuls of currants; 6 green gages; 12 cherries; half a medium-sized pear; corresponding amounts of other fresh fruits.

Table III.

Third Group: Conditionally Allowable Foods.

The condition under which dishes from the following table are permitted is that an equivalent shall be deducted from the allowance of bread. The amounts given below are the equivalents of 50 grams of white bread, containing about 30 grams of starch. Advantage is taken of the fact that larger amounts of certain carbohydrates (cane sugar, milk sugar, fruit sugar, etc.) may be allowed than of starch. Some of the dishes given in the preceding table appear again here because, if they are eaten in larger quantities, an account must be taken of the carbohydrate which they contain.

1 litre of milk (sweet, sour or buttermilk).

1½ litre of kumyss (prepared in the Russian way).

1 to 1½ litre of kephyr (fermented for at least two days and prepared without the addition of sugar).

1 litre of cream.

60 grams of rye bread, graham bread, or Hamburg pumpernickel.

65 grams of Westphalian pumpernickel.

100 grams of aleuronat bread, prepared after Ebstein's formula (containing 27.5 per cent. of carbohydrate and 32 per cent. of vegetable albumin; the aleuronat breads are very variably compounded).

35 grams of zwieback and simple coffee-cakes (made without sugar).

30 grams of English cakes of various sorts.

30 grams of "eichel cacao" (Stollwerck's).
50 grams of chocolate (Stollwerck's).
40 grams of chocolate (French make).
40 grams of chestnuts shelled, or 60 grams unshelled.
35 grams of cane sugar, brown sugar, or rock candy.
35 grams of sweet preserves.
40 grams of fruit sugar.
40 grams of milk sugar.
50 grams of fruit jam.
40 grams of honey.
40 grams of flour, wheat, rye, barley, buckwheat, millet, or oat, or corn-meal.
45 grams of bean, pea, or lentil flour.
35 grams of starch preparations, potato, wheat, or rice starch, tapioca, sago, maizene, mondamin, etc.
35 grams of rice.
35 grams of farinaceous preparations, nudel, maccaroni, oatmeal, grits, barley.
50 grams of lentils, peas, beans, weighed dry.
100 grams of green peas.
180 grams of new potatoes.
140 grams of winter potatoes.
120 grams of apples, pears, green gages, plums, damsons, mirabelles, apricots, cherries, grapes.
200 grams of strawberries, raspberries, gooseberries, mulberries, currants, blackberries, whortleberries, blueberries.
3 peaches.
40 grams of raisins or dried dates.
50 grams of figs.
3 bananas.
A handful of walnuts, hazelnuts, almonds, or Brazil nuts.
$\frac{2}{3}$ litre of beer of any sort.
$\frac{1}{6}$ litre of sweet wine.

Table IV.

Fourth Group: Especially Valuable Foods.

The great value of the following articles, of which, however, there is but a small choice, is due in part to the high percentage of albumin and in part to that of fat. The proportion of albumin and fat is given for each 100 grams of the food substance. Some contain carbohydrates also, the percentage of which is given for the sake of completeness, but its nutritive value is not counted.

100 Grams.	Albumin.	Fat.	Carbo-hydrate.	Calorie value.
Vegetable oil	..	100	..	930
Butter	1	85	0.5	830
Bacon (salt or smoked)	10	76	..	748
Devonshire cream	2	57	2	538
Cream cheese (Gervais, Neufchâtel, Stilton, Stracchino, etc.)	19	41	1	451
German sausage (Cervelatwurst)	18	40	..	446
Ham	25	36	..	437
Cheddar cheese	28	33	2	422
Fat pork	14	37	..	400
Smoked ox-tongue	24	32	..	396
Fatty cheese (average)	25	30	1.5	381
Yolk of egg	16	31	0.5	354
Fat goose	16	30	..	345
Fat beef and mutton	17	29	..	337
Brie cheese	19	26	1	320
Fresh-water eel	13	28	..	312
Smoked mackerel	19	22	..	382
Caviar	31	16	..	276
Cream	4	23	4	230
Fat salmon (fresh or smoked)	22	13	..	210
Hens' eggs (weighed with the shell)	12	10	0.5	142

EXAMINATION OF DIABETIC URINE.

I. Grape Sugar.

Several tests should always be employed in order to determine with certainty the presence of grape sugar. Some of these are very easily made and serve for a provisional diagnosis, others demand more time and may be employed to confirm this provisional diagnosis. If albumin is present in the urine, it should be removed by boiling and filtering before the test for sugar is made.

1. *Provisional Tests.*

For this purpose Trommer's and Nylander's reduction tests and Moore's reagent are the most suitable.

a. Trommers' Test.—Reagents: (1) A 10-per-cent. solution of caustic soda or potash; (2) A 5-per-cent. solution of copper sulphate.

Principle: Copper sulphate when heated with glucose in an alkaline solution is reduced to red oxide of copper (Cu_2O) and yellow oxide of copper ($Cu_2O_2H_2$).

Application: 5 c.c. urine and 5 c.c. solution of caustic soda are mixed in a test-tube. Then the copper sulphate is added a drop at a time until on shaking it is no longer dissolved. If sugar be present

the cold fluid assumes a dark-blue color, and when heated, even before the boiling-point is reached, an orange-red precipitate is formed. If on heating and boiling the fluid is only colored yellow without any orange-red precipitate, or if the yellow precipitate is thrown down only on cooling, the presence of sugar may be suspected but is not actually proven; for usually then the yellow coloration of the fluid and the precipitation of copper oxide are due to the presence of other reducing substances.

In urine which contains few other organic substances than sugar, the test will show 0.2 to 0.3 per cent. of sugar; but when there is an abundance of uric acid, creatinin, and other amido-combinations, or of free ammonia, the test will show with certainty not less than 1 per cent. The delicacy of the reaction is increased if the urine is previously filtered through animal charcoal.

Partly on account of its want of delicacy and partly because of a certain capriciousness, the reasons for which are not always very evident, this reaction does not really deserve the popularity which it enjoys. After having compared Trommer's and Nylander's tests in every case of saccharine urine which I have examined for many years, I have come to the conclusion that the latter is by far preferable.

b. Nylander's Test.—Reagents: 4 gm. sodium tartrate are dissolved in 100 c.c. of a 10-per-cent. solution of caustic soda, to which 2 gm. subnitrate of bismuth are added. The mixture is heated up to 50° C. (122° F.), and filtered when cool. The reagent may be kept unaltered for months.

Principle: Subnitrate of bismuth in contact with grape sugar in a boiling alkaline solution is reduced to black metallic bismuth.

Application: 10 c.c. of urine and 1 c.c. of the reagent are boiled for two minutes. If sugar be present there is a brown to black coloration of the fluid or precipitate, metallic bismuth being thrown down. If the dark coloration takes place gradually as the fluid cools, the presence of sugar is not proven. The reaction takes place when sugar is present in the proportion of 0.1 per cent. But as other substances (in particular medicinal and vegetable substances which are excreted in the urine) give rise to the same reaction, we cannot be sure when it is obtained that sugar is always present. The absence of a reaction is, however, positive proof that sugar is not present in the above-mentioned proportion.

c. Moore's Test.—3 c.c. of a 10-per-cent. solution of caustic potash and 10 c.c. of the suspected urine are thoroughly mixed together. The upper portion of the fluid is then heated and boiled for at least one minute. If sugar be present in the proportion of at least 0.5 per cent. the heated layer becomes of a brown color which grows

darker with further heating. Normal urine shows under the same conditions only a dark-yellow coloration.

2. *Positive Tests.*

The tests above described are only provisional, as the reaction may be caused by the presence of other substances than sugar. If all three tests, especially Nylander's, give a negative result then any further test is unnecessary. If they all give positive results the presence of sugar is at least very probable. Nevertheless it is better to have the evidence of other tests. This is absolutely necessary when the provisional tests have given uncertain or contradictory results.

a. The Fermentation Test.—To 30 c.c. of the suspected urine a piece of ordinary yeast the size of a pea (or better a small quantity of a pure culture of saccharomyces apiculatus) is added, and the whole well shaken. Then the urine is poured into a so-called "fermentation tube" and set aside in a warm place (20° to 30° C.—68° to 86° F.). If much sugar be present (0.5 per cent. or more), a large quantity of gas (carbonic acid) will have collected by the end of two hours at the upper extremity of the tube; if but little sugar be present, we shall have to wait from five to eighteen hours. The formation of gas is very evident when not more than 0.15 per cent. of sugar is present in the urine.

It is advisable, for comparison, to place another glass containing normal urine and yeast alongside of the first one, for the yeast itself often contains traces of sugar. In that case there will be a small bubble of gas at the top of the tube containing normal urine, but that in the other tube, containing saccharine urine, will be much greater in amount.

The gas set free is carbonic acid, as the yeast fungus splits up the grape sugar into alcohol and CO_2. If caustic potash be added to the fermented urine the gas will disappear as the potash seizes upon the carbonic acid.

b. E. Fischer's Phenylhydrazin Test.—10 c.c. of urine and 2 drops of a saturated solution of neutral acetate of lead (sugar of lead) are mixed together and then filtered. The filtrate is acidulated with one drop of glacial acetic acid, and to it are added a piece the size of a pea of phenylhydrazin and one the size of a bean of acetate of sodium. The test-tube is then placed in a water-bath for an hour and heated. At the end of this time, if sugar be present, there will be a yellow precipitate formed in which there can be seen under the microscope a cluster of beautiful, long, yellow, needle-shaped crystals. These needles consist of phenylglycosazon. This test gives positive results in the presence of only 0.05 per cent. of sugar. It must be remem-

bered, however, that it is only these yellow, needle-shaped crystals that are indicative of sugar.

c. Rubner's Test.—10 c.c. of urine are mixed with an equal amount of a concentrated solution of neutral acetate of lead and then filtered. To the filtrate ammonia is added drop by drop until a thick cheesy precipitate is formed. It is then cautiously heated up to not more than 80° C. (176° F.). When grape sugar is present, the previously white precipitate is colored a beautiful rose-red. Further heating changes the color to a coffee-brown. A positive reaction is obtained when sugar is present in the proportion of at least 0.25 per cent.

d. The Circumpolarization Test.—Solutions of grape sugar have the property of turning the plane of polarized light to the right. In order to examine the urine for this property we may use either the saccharimeter of Soleil-Ventzke or the so-called half-shadow apparatus of Laurent, Lippich, and others. Marked dextrorotation of polarized light always points to the presence of grape sugar; a slight dextrorotation may be caused by milk sugar (in lying-in women), by compounds of glycuronic acid often present in the urine, or by many medicinal substances. On the other hand saccharine urine may lose the property of dextrorotation when at the same time levorotatory substances are present in the urine (oxybutyric acid, levulose, and many drugs, such as benzosol).

e. Differentiation of Milk Sugar from Grape Sugar.

	Grape sugar.	Milk sugar.
Trommer's test.....	Positive.	Positive.
Nylander's "	Positive.	Positive.
Moore's "	Positive.	Positive.
Fermentation test....	Positive.	Negative.
Phenylhydrazin test .	Yellow needles, with a melting point of 204° to 205° C.	Globular collections of yellow needles, with a melting point of 200° C.
Rubner's test	Cherry-red color.	Orange-red or brown color.

3. *Quantitative Estimation of Grape Sugar.*

a. By Means of Polarization.—The different saccharimeters either indicate directly on a scale the percentage of sugar in the urine or mark only the degree of rotation of the polarized light. In the latter case an accompanying table shows to what percentage of sugar the degree of rotation corresponds. A description of the apparatus is given in every text-book on the technique of physiological chemistry.

b. By Means of Fehling's Solution.—Reagents. (1) A solution of 34.639 gm. pure crystallized sulphate of copper in 500 c.c. water; (2) 173 gm. sodium tartrate are dissolved in 350 c.c. pure caustic soda of

a specific gravity of 1.14, and water is added to bring the entire volume up to 500 c.c. (3) Immediately before being used, a mixture is made of 10 c.c. of each of the two solutions. We then have 20 c.c. of a dark blue fluid which is called "Fehling's solution."

Principle: Upon boiling a thin solution of grape sugar with Fehling's solution, the copper sulphate is reduced to red copper oxide, exactly 0.1 gm. of grape sugar being necessary to reduce completely 20 c.c. of Fehling's solution.

As this condition is met with only when the saccharine solution contains between 0.5 and 1 per cent. of sugar and when it is added very rapidly to the Fehling's solution, it is therefore necessary: (1) by means of a preliminary test with Fehling's solution or by polarization, to estimate approximately the percentage of sugar, and then to dilute the urine for the definite test so that it contains only from 0.5 to 1 gm. of sugar in 100 c.c.; (2) to add the Fehling's solution gradually to the diluted urine. If, for example, it were found that 20 c.c. of the diluted urine are needed to obtain the complete reaction, then in a second test 20 c.c. of urine are to be added quickly to the Fehling's solution. The end reaction does not take place, and some tenths of a cubic centimetre, say 0.5 c.c., must be added in order to obtain it. In this case, therefore, 20.5 c.c. of the diluted urine would exactly correspond to 20 c.c. of Fehling's solution, that is to say would contain just 0.1 gram of grape sugar. If the urine had previously been diluted ten times we should have the following computation:

$$20.5 \text{ c.c. of diluted urine contains } 0.1 \text{ gm. grape sugar.}$$

$$1. \quad " \quad " \quad " \quad " \quad " \quad \frac{0.1}{20.5} \quad " \quad " \quad "$$

$$1. \text{ c.c. of undiluted urine contains } \frac{0.1 \times 10}{20.5} \text{ gm. grape sugar.}$$

$$100 \text{ c.c. of undiluted urine contains } \frac{0.1 \times 10 \times 100}{20.5} = 4.88 \text{ gm. grape sugar.}$$

Application: 20 c.c. of Fehling's solution are diluted with 80 c.c. of water and heated to boiling in a glass cucurbit having a capacity of about 200 c.c. The urine is now added from a burette to the boiling fluid. After each addition of urine the urine is boiled for a minute. The addition of urine and the boiling are continued until the fluid, which becomes turbid with the precipitated red oxide of copper, ceases to be distinctly blue. When the color of the boiling fluid can no longer be clearly recognized, the cucurbit is removed from the fire after each addition of urine and subsequent boiling and held up between the eye and the window. There will then be seen, as soon as the precipitate begins to sink, a light layer immediately

below the surface of the fluid. As long as this ring appears blue or bluish-green the reduction is not completed, that is, a sufficient amount of urine has not been added; as soon as the ring is colorless the reduction is complete; when the ring assumes a yellow color too much urine has been added to the Fehling's solution.

This method gives, after some practice, very distinct results, and is in my opinion superior to all the other modifications of Fehling's titration method.

c. By Means of Aerometry and Fermentation.—The specific gravity of saccharine urine is reduced by fermentation, as the heavy sugar is taken away and light alcohol is formed in the fluid. Roberts and others have determined experimentally to what percentage of sugar a definite decrease in specific gravity following fermentation corresponds. The method is easily carried out and gives approximately accurate results if (1) the specific gravity is obtained both times with the same temperature, (2) the aërometers are very exact, and (3) the yeast is absolutely pure.

Application: After the specific gravity has been ascertained, the yeast is added and the mixture is set aside in a temperature of from 25° to 30° C. (77° to 86° F.). The fermentation should be carried on until the urine gives no sugar reaction, and then the specific gravity is again taken. The difference of specific gravity multiplied by 430 gives the percentage of sugar in the urine.

Example: Specific gravity before fermentation..... 1.040
" " after " 1.018

Difference 0.022
Percentage of sugar.....0.022 × 430 = 9.46

II. Acetone.

To 100 c.c. of urine are added five drops of hydrochloric acid, and the mixture is then distilled. A few cubic centimetres of the distillate are now treated with three drops of caustic potash and a few drops of compound solution of iodine. If acetone is present a light yellow precipitate of iodoform, having the characteristic odor of this substance, is thrown down.

In a quantitative analysis we have to determine not only the amount of already existent acetone but also of that formed by the splitting up of diacetic acid. One drop of glacial acetic acid is added to 100 c.c. of urine and distilled, the receiver and tube being kept very cool, until three-quarters of the entire amount has passed over. This distillate is treated with five drops of dilute (25 per cent.) sulphuric acid, and after a few crystals of urea are added is again dis-

tilled, the receiver and tube being cooled as before. To the second distillate caustic potash is first added and then compound solution of iodine in excess. A precipitate of iodoform is thrown down which is collected, at the end of six hours, on a weighed filter and washed with distilled water. After the filter and precipitate have been allowed to dry in the air they are placed in an exsiccator with sulphuric acid, and weighed at the end of one and one-half to two hours. One gram of iodoform represents 0.147 gm. acetone. By reason of the volatility of iodoform the loss of a small amount (one or two per cent.) cannot be avoided. This small error may be ignored, but there is another source of error that is of more importance; for when the patient has been taking large doses of alcohol a certain amount will always pass off in the urine and will give the same reaction as acetone in the distillate.

III. Aceto-Acetic Acid.

Urine which contains aceto-acetic acid becomes of a Burgundy-red color upon the addition of a few drops of a solution of ferric chloride. The first few drops of ferric chloride throw down a dirty grayish-yellow precipitate of phosphate of iron in many specimens of urine, but this is again dissolved by the addition of more of the reagent. The reaction is much more beautiful and distinct if a solution of neutral acetate of lead (10 drops of the concentrated solution to every 10 c.c. of urine) be first added. The white precipitate thus formed is filtered out and the test then applied to the filtrate.

It should be remembered that the same color reaction is obtained in the urine after the administration of salicylic acid, antipyrin, salol, phenocol, salipyrin, and many other drugs.

IV. Beta-Oxybutyric Acid.

A formal test for oxybutyric acid need be made only when certain provisional tests have furnished a presumption of the presence of this substance. The presence of the acid is rendered probable:

1. When Fehling's titrate method gives evidence of the presence of considerably larger amounts of sugar than does the polarization test. Grape sugar rotates the plane of polarization to the right, oxybutyric acid to the left; when, therefore, oxybutyric acid is present in considerable proportions, a part of the dextrorotatory power of the grape sugar is nullified, or it may even be that there is so much oxybutyric acid that the plane of polarization is actually rotated to the left.

2. When the urine, after complete fermentation with yeast, is found to be levorotatory.

3. When the urine, after precipitation with basic acetate of lead and ammonia, is levorotatory. By means of these reagents the sugar is practically entirely removed, but the oxybutyrate of lead remains in solution and passes through with the filtrate.

The application of these methods, when it gives a positive result, renders the presence of oxybutyric acid very probable. But we must be sure that the patient has not taken large amounts of benzosol, for this substance also rotates the plane of polarization to the left. The presence of levulose (after the consumption of a large amount of fruit sugar) does not invalidate this presumption, if the fermentation or lead-and-ammonia tests have been employed.

In order to determine with absolute certainty the presence of oxybutyric acid and to estimate its quantity we must resort to the method of Minkowski (as described in the paper of H. Wolpe in the *Archiv für experimentelle Pathologie und Pharmakologie*, Bd. XXI., S. 140, 1886) or to that of Külz (*Zeitschrift für Biologie*, Bd. XXIII., S. 321, 1887).

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RHEUMATISM.

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RHEUMATISM.

The term rheumatism was first employed to describe morbid conditions characterized by mucous defluxions, conditions to which we now apply the term catarrh. The disease which we now call rheumatism was originally confounded with gout, and the two were described together under the common name of arthritis. Sydenham was the first to distinguish between the two maladies and to give anything like an accurate description of rheumatism properly so-called.

Varieties and Symptoms.

The disease is generally described as occurring in three forms, the acute, the subacute, and the chronic. For clinical purposes this is as convenient a classification as can be given.

Acute Rheumatism.

Acute rheumatism, or rheumatic fever, commences with a feeling of cold, occasionally with a distinct rigor, succeeded by a sense of weakness and general malaise. These symptoms are accompanied by aching pains in different parts of the body, especially in the limbs. These quickly increase in severity and are seated chiefly in the large joints, which soon become swollen and very tender. The temperature rises at the same time, and the skin is covered with a free perspiration which has a sour and disagreeable odor. Acute pain in the affected joints is the dominating feature of acute rheumatism; and the inflammation of the joints which causes this suffering is the most prominent and characteristic lesion of the fully developed disease. As a rule it is confined to the large joints—the knee, ankle, wrist, elbow, shoulder, and hip joints being attacked with a frequency which corresponds very much to the order in which they have been enumerated. Of the small joints the knuckles are most apt to suffer. In striking contrast with what is observed in gout, the joints of the foot, other than the ankle, are rarely affected.

The local symptoms of this lesion are pain, swelling, and great tenderness of the inflamed joints. Occasionally there is redness of

the surface, but such redness is less marked and less common than it is in gout.

The inflammation shows a decided tendency to shift from joint to joint. This alternation of pain and freedom from pain may be experienced by most of the large joints of the body more than once during an attack of acute rheumatism. The invasion of fresh joints is not always accompanied by diminution of the inflammation of those already affected; though occasionally there is noted what seems to be, and is by many regarded as a true metastasis—a sudden passage of the inflammation from one joint to another.

Febrile symptoms are marked. The pulse and respirations are increased in frequency. The temperature varies from 101° to 104° Fahr., but has no distinctive range; the general course of the fever being irregular rather than continued. While the ailment continues there is no time at which the patient is free from fever or pain, but there may be many ups and downs in the course of both before the ailment comes finally to an end.

The skin is very active in acute rheumatism: the surface is usually bathed in a profuse perspiration which is a source of much discomfort. It has a sour, disagreeable odor and an acid reaction. The naturally alkaline saliva may also be acid. The urine is hyperacid, scanty, high-colored, and on standing throws down a copious deposit of urates. Its specific gravity is high, and it contains an increased quantity of urea. The bowels are constipated; the tongue is coated with a thick white fur; the appetite is gone, and there is considerable thirst. The patient's condition in a severe case is pitiable in the extreme. He lies on his back unable to move, the least effort to do so causing intense pain. The perspiration trickles down his face, but he cannot raise his hand to wipe it away. Even the weight of the bedclothes cannot be borne. He dreads the approach of his friends, screams with agony at the least touch, and sometimes even without such a cause. His expression is that of intense suffering and abject helplessness. He gets no rest. His one desire is to have some relief from pain.

The disease varies in duration. When uninfluenced by treatment the acute symptoms generally last for two or three weeks. But the fully developed disease, as here described, is never seen nowadays, so efficacious is treatment in arresting its course; and those who have entered the profession since 1876 can have no adequate idea of the acute and prolonged suffering which characterized an attack of acute rheumatism left to run its natural course.

During its course there is a marked tendency to inflammation of the structures of the heart. This constitutes the chief danger and

anxiety of the illness, for the heart when once affected is apt to be permanently damaged; while in not a few cases the cardiac inflammation proves directly fatal in its acute stage. The great majority of cases of acute rheumatism do recover. The prognosis, therefore, is favorable.

In some cases, fortunately in few, the temperature runs up to 106°, 108°, or even 110°. With this high temperature there are associated alarming nervous symptoms. This constitutes that form of the disease to which, from its fatality, the term "malignant" has been applied. It is now generally described under the name of rheumatic hyperpyrexia. To its consideration we shall by and by return.

Subacute Rheumatism.

This is a milder form of the same disease, and presents the same symptoms and features in a minor degree. It comes on more gradually, generally like an ordinary cold, and usually without any initial rigor. Fewer joints are affected at one time; the inflammation of the individual joints is less severe, the pain is less exquisite, and the swelling less marked—though both are distinct enough. The joint affection shows the same tendency to shift and vary its seat; but the patient is less helpless, and his general condition not so acutely distressing. There is the same acid perspiration, but not so much of it. The heart is apt to suffer in this as in the acute form, but not quite so frequently. When it is affected the inflammatory action partakes of the generally milder character of the ailment and is more rarely a source of immediate danger. The remote consequences are apt to be the same in both. The temperature ranges from 99° to 101°. Well-marked cases of subacute rheumatism run by insensible gradations into mild cases of the acute form of the disease. The treatment of both is the same.

Chronic Rheumatism.

This name is loosely applied to many ailments not really of rheumatic origin. Almost any obscure and obstinate pain which is not traceable to some other agency is apt to be attributed to chronic rheumatism. Under this head there thus come to be ranked many aches and ailments which, not being of rheumatic origin, have no claim to the title. Chronic rheumatism properly so-called is a milder form of the subacute variety in which there is not sufficient local inflammation to lay the patient up, or to raise the temperature.

Just as the acute runs into the subacute, so the subacute runs into the chronic by insensible gradations. It is sometimes the precursor,

often the sequence, of an acute or subacute attack. It also exists independently of them. "Remarquons d'abord qu'à un degré très-léger, et lorsqu'il n'occupe qu'un petit nombre d'articulations d'un volume peu considérable, le rhumatisme articulaire est souvent apyrétique, à quelque période qu'on examine les malades" (Bouillaud).

The malady is characterized by the occurrence of pains, obstinate in nature, and sometimes shifting in character, affecting the joints, muscles, and fibrous aponeuroses. The affected parts may be somewhat tender to touch, but are not, as a rule, distinctly swollen. The pain is increased by damp and cold. It often disappears in fine and returns in wet weather. Unless the patient is in easy circumstances he may never be confined to the house, and never consult a medical man, but may go about his daily work until he gets better, or until the onset of an acute or subacute attack compels him to lay up. It is a troublesome ailment which frequently lasts off and on for months. During its continuance there is often laid the foundation of future cardiac troubles. The temperature may now and then rise to 99°, or even a little higher—making the case for the time subacute; but generally it is normal. The pulse is not quickened.

In the age, in the personal and family history of the patient, in the seat of the pain, in its shifting character, and in the occasional slight rise of temperature, we have the best means of distinguishing true chronic rheumatism from the other ailments, gouty, arthritic, and neuralgic, with which it is so often confounded. It is of the utmost importance that such a distinction should be made, for on the accuracy of our diagnosis depends our ability to relieve the patient, and mitigate his sufferings.

Diagnosis.

The diseases for which acute and subacute rheumatism are most apt to be mistaken are acute gout, acute rheumatoid arthritis, pyæmia, and gonorrhœal rheumatism. As a rule the differential diagnosis presents no serious difficulty.

Acute gout is a disease of mature years; acute rheumatism a disease of youth. Gout generally affects only one joint; rheumatism several. Gout attacks chiefly the small joints; rheumatism the large. In acute gout the skin over the affected joint is red and glistening; in acute rheumatism, as a rule, redness of the surface is not marked. In acute gout the skin is dry and unperspiring; in acute rheumatism it perspires very freely. In acute gout the blood contains uric acid; in acute rheumatism it does not. Acute gout is not benefited by salicin and salicylic acid; acute rheumatism is speedily cured by them. Acute gout is much less apt to affect the heart.

Acute rheumatoid arthritis resembles subacute rather than acute rheumatism. It is distinguished from it by the following peculiarities: Acute rheumatoid arthritis is a comparatively rare disease. It occurs chiefly among young women whose health has already been impaired by some debilitating cause, generally menstrual or uterine disturbance, or prolonged lactation. It comes on more gradually than rheumatism. It attacks the small joints as frequently as the large. It shows no tendency to shift from joint to joint. The skin does not perspire profusely as in acute rheumatism. The urine is generally pale in color and of low specific gravity. It is a more obstinate ailment, and does not yield to remedies which speedily cure rheumatism. It does not tend, like this, to affect the heart.

Pyæmia.—Cases of pyæmia sometimes occur in which the presence of joint inflammation, possibly also of endocardial inflammation, of febrile symptoms, and of free perspiration give to the ailment some resemblance to a case of acute rheumatism.

The diagnosis is not difficult. In pyæmia there is the existence of some wound or other lesion to explain its occurrence; the rigors are more marked; the joint inflammation does not shift about; the perspiration is not acid; and the general symptoms are of a more markedly typhoid type. Should we fail to make a diagnosis by these means, the doubt is not unlikely to be soon set at rest, if the case be one of pyæmia, by the onset of alarming typhoid symptoms and a speedily fatal result.

Gonorrhœal rheumatism occurs in connection with gonorrhœa. It is not accompanied by the same amount of febrile disturbance as acute or even subacute rheumatism. It affects fewer joints, has a special preference for the knee, and does not show the same tendency to shift about. Acid perspirations do not occur; and it does not tend to affect the heart. Remedies which speedily cure true acute rheumatism have no influence on the gonorrhœal form of the disease.

There is another morbid condition to which the term rheumatism is usually applied, but which is more properly a sequence of rheumatism than a distinct form of the disease; and which is so apt to be mistaken for the subacute and chronic forms of the malady, that it will be well to refer to it here. When a man has suffered from repeated rheumatic attacks, especially when these have followed each other in quick succession, there is apt to be induced a state of chronic thickening of the fibrous textures involved in the disease. The nature of the change, and the influence exercised by it on subsequent rheumatic attacks, will be considered hereafter. Meantime its existence is indicated with the object of pointing out that this condition, though of rheumatic origin, exists, when developed, independently of the

rheumatic poison; and may give rise to symptoms indistinguishable from those caused by it—pain and stiffness of the joints. The importance of recognizing its existence will be apparent when we come to consider the question of treatment.

The Duration of Rheumatism.

Next to pain and the heart complications one of the most noticeable features of rheumatism is its prolonged duration when not influenced by treatment. That the chronic form should be thus characterized is no more than one would expect in an ailment to which the term chronic is applicable. It is in connection with the acute and subacute forms that this feature calls for special notice. The long duration of acute rheumatism has been remarked by every one who has written on the subject. It is this which imparts, or used to impart, to the ailment many of its horrors.

Till very recently it was no uncommon thing for the disease to last for months, and only in exceptional cases did the patient have less than three weeks of suffering. "In my last attack I was in constant agony for six weeks." "Every attack has laid me up for three or four months." Such till within very recent years were the common experiences of those subject to the disease. A considerable variety in the duration of different cases has always been noted as a leading feature in its natural history. Some are exceptionally long; others exceptionally short. Hence the mean duration of the malady varies with the varying experience of different observers. But all agree in calculating this by weeks rather than by days.

Pinel says that it lasts from seven to sixty days.

Scudamore remarks that "In a case of which the issue is favorable, the fever and pains are brought to a close at the end of the third week; and in slight attacks at an earlier period; but when the course of the disease is untoward, a period of two months scarcely serves to exhaust its power in producing even acute symptoms."

"How long," says Macleod, "a case of acute rheumatism of medium severity might endure if left to itself, I am unable to say; but, with the common methods of treatment, probably five or six weeks may be about the average duration of rheumatic fever."

According to Chomel, the disease rarely disappears before the twentieth day, and is sometimes prolonged for three months.

Bouillaud stated that under the modes of treatment adopted up to the time at which he wrote (1840) the mean duration of acute rheumatism was forty to fifty days; but that under the influence of the treatment to which he had recourse (bleeding *coup sur coup*) it was reduced to less than half that time, *i.e.*, about three weeks.

Fuller says that his own observation led him to believe "that even when unattended by any internal affection, the disease, under ordinary methods of treatment, endures from four to five weeks."

Garrod puts it at "from ten days to three or four weeks."

Niemeyer gives the duration of mild cases as "one or two weeks;" and of severe ones as "many weeks."

Senator says that "as a rule acute polyarthritis runs its course in from three to six weeks."

Lebert gives the statistics of 108 cases of which—10 lasted from 5 to 15 days, 58 lasted from 16 to 35 days, 32 lasted from 36 to 55 days, and 8 lasted from 56 to 80 days.

In Dr. Bristowe's work on "Practice of Medicine," published in 1876, the duration of acute rheumatism is thus referred to: "There is no definite limit to the duration of acute rheumatism. Sometimes the patient recovers completely in the course of a day or two, or of a week; more commonly the disease persists for several weeks; and not unfrequently it becomes chronic, or is continued by successive relapses for a much longer period than that."

In the St. Thomas' Hospital reports for 1872 Dr. Peacock gives a statistical account of the cases treated in that hospital during the previous year. He there states that the largest proportion of cases recovered in the fourth week. This may be accepted as consistent with general experience.

With regard to hospital statistics on this subject, however, it has to be remarked that the proportion of acute to subacute cases is larger in private than in hospital practice. The explanation of this is to be found in the difficulty or even impossibility of removing a very acute case to hospital during its very acute stage, and such cases are very acute from the commencement. Over and over again have I seen cases of subacute rheumatism brought into hospital with a history of acute rheumatism of several weeks' duration. The explanation of the delay in sending them generally was that they were too ill to be moved. And one can quite see the force of that, for a man who cannot bear the weight of the bedclothes, who screams with agony at the least shake of his bed, or at the lightest touch by a friend, is one whom it would be impossible to subject to the movement and disturbance inseparable from conveyance to another locality.

For this reason very acute cases are more often seen in private than in hospital practice, and hospital statistics are to be regarded as giving to acute rheumatism a milder aspect and shorter duration than would be got from similar statistics taken from private practice. For the same reason Dr. Peacock's statistics probably under- rather than over-state the mean duration of all cases of acute rheumatism.

Such are the statements of the best authorities. All agree in ascribing to acute rheumatism a mean duration of several weeks. And this coincides with the experience of every practitioner. No one who saw much of the disease before the days of the salicyl treatment, can fail to recall, on the one hand, cases in which the patient, to the delight of himself and attendants, got over the attack in one or two weeks; and, on the other hand, cases which dragged on their weary and painful course for six or eight weeks and even more.

The duration of the disease is determined by the duration of pain, its most prominent and characteristic feature. Pain, of course, is only one symptom, but it is that which is most characteristic, which is most complained of, which continues so long as the rheumatic poison exercises its action on the joints, and without which rheumatism cannot be said to exist in the joints. The temperature may decline, the pulse may fall, the perspirations may cease; but so long as pain remains in any of the joints, the patient is not convalescent, and may have a re-accession of all his symptoms.

Nowadays we have in the thermometer a delicate means of determining the duration of the febrile symptoms which are an essential characteristic of acute rheumatism. It is found that the objective evidence thus got, accords very closely with the subjective evidence derived from the patient's feelings on which our fathers relied. The temperature falls and rises with the decrease and increase of pain and swelling in the joints, but rarely comes permanently to the normal standard till the joint pain disappears. The cases in which the joint pains persist after the normal temperature has been reached, are those in which the chronic form of the disease follows in the wake of the acute, and in which this sequence of events imparts to the attack an unusually prolonged duration, if we calculate this by the duration of the pain alone. This grafting of the chronic on to the acute form explains the long duration of those cases in which acute rheumatism is said to have lasted for several months. Such cases commenced as acute rheumatism, gradually passed into subacute, and still more gradually into the chronic form. So insensible are the gradations by which the one form runs into the other, that with the thermometer it is difficult, and without it impossible, to say exactly when acute becomes subacute, and subacute chronic. It is seldom, however, that a case remains acute for more than three weeks. It may be acute for that time, subacute for three or four weeks more, then gradually and without cessation of pain pass into the chronic form, and so remain for many weeks—the whole duration of the ailment being several months. It is one attack all through; but it is not acute rheumatism during its whole course.

The chronic course of such cases may be interrupted and varied by subacute exacerbations of longer or shorter duration; serving to show that the chronic form of the disease owns the same causation as the acute and subacute forms which precede and follow it. These very prolonged cases are exceptional. Generally the febrile symptoms and the pain decline and disappear about the same time.

The authorities and statements which have been quoted existed and were made before 1876, the year in which the salicyl compounds were introduced for the treatment of acute rheumatism. When we come to consider the duration of the malady under this treatment, it will be seen how vast are its benefits. For whereas this duration was formerly calculated by weeks it is now estimated by days. Taking pain as the index of its continuance, it will be found that when the salicyl treatment is properly applied the disease lasts as many hours as it formerly did days, or as many days as it formerly did months. For in many cases the pain is now more effectually and surely relieved in one day than it formerly was in one month. The temperature, too, falls to the normal very soon after the pain is abolished.

The Seat of Rheumatism.

Though some difference of opinion is found among old authors as to the exact seat of rheumatism—Latham, for instance, regarding the lymphatics, and Carmichael Smyth the muscles, as being specially involved—the malady is nowadays generally believed to have its seat chiefly in the fibrous and serous tissues.

And there is good reason for this belief. The rheumatic poison is found to exercise its action on, and almost exclusively on, particular organs and textures in which these tissues predominate, and which seem to have no other feature in common. The joints, muscles, and heart are the parts chiefly involved. In the case of the joints, it is not the osseous, but the fibrous and serous, elements—the capsules, ligaments, tendons and tendinous sheaths, and the synovial membranes, which suffer. So with the heart; the white fibrous structure of the rings and valves and the serous investing membrane suffer much more than the muscular substance.

Fibrous or serous tissue appears to be requisite to the action of the rheumatic poison and to the development of rheumatism. But all fibrous and serous textures are not equally apt to suffer. The periosteum is a fibrous membrane, and a most abundant one; but it suffers seldom. The dura mater is so too, but it is rarely the seat of rheumatism. The liver, spleen, kidney, and uterus have much fibrous tissue in and around them; but the membranes which this

fibrous tissue forms do not suffer as do the fibrous textures of the joints and heart.

Then there are many joints which enjoy a comparative immunity from the disease. The small joints of the fingers are not often affected; the small joints of the toes more rarely still. One seldom meets with true rheumatic inflammation of the articulation of the lower jaw, or of the joints of the atlas and axis. And I never saw, or heard of, a case in which the articulations of the ribs were involved. And yet all these joints have ligaments, and fibrous and serous tissues. The pleura, peritoneum, and arachnoid are serous membranes; but they do not suffer as the pericardium does. With all these exceptions before us we cannot, without hesitation, accept the view that rheumatism is essentially a disease of the fibrous and serous tissues. It is only a part of these tissues which shows a special susceptibility to the action of the rheumatic poison. The fibrous membranes which surround the brain and spinal column, the fibrous membrane which covers the bones externally, and those which invest and give support to the liver, spleen, kidneys, and uterus, far exceed in quantity the fibrous textures of the large joints and of the heart; and yet, for once that rheumatic inflammation occurs in any one of these membranes it occurs many hundred times in the ligaments of the large joints.

The serous investing membranes of the brain, of the lungs, and of the abdominal organs, far exceed in extent the corresponding membrane of the heart; but for once that any of them is the seat of rheumatic inflammation the pericardium suffers a hundred times.

In structure all white fibrous tissue is very much alike; but in function it varies much. The chief of its functions are (1) to support entire organs, (2) to bind together and give support to their constituent parts, (3) to control and regulate movement.

That which supports entire organs is instanced in the fibrous coverings and appendages of the liver, spleen, uterus, etc. That which binds together and gives support to their component textures, is instanced in ordinary connective tissue. That which is engaged in controlling and regulating movement, is exemplified in the fibrous textures of the joints. It is this last form of white fibrous tissue which is specially involved in rheumatism.

One of the chief functions of serous membrane is to facilitate movements. In some organs which are provided with a serous investment the movements are so slight that the membrane has no very active function to perform in this way. The only serous membranes engaged in really active work of this kind are the investing membrane of the heart, and the lining or synovial membranes of the larger joints, which in function are to be regarded as serous membranes.

Now putting these various facts together—finding that many of the fibrous and serous tissues of the body are not subject to rheumatism, but that the disease is limited almost entirely to such fibrous and serous tissues as are habitually engaged in facilitating, regulating, and restraining active movement—we cannot fail to see that the seat of rheumatism is not fibrous tissue in general but such fibrous tissue as is habitually engaged in controlling and regulating movement; and not serous textures in general but such serous textures as are habitually engaged in facilitating free and active movement. In other words, rheumatism is essentially a disease of the motor apparatus, and the chief seats of the morbid process are the fibrous and serous structures of that apparatus.

There are fifteen common seats of rheumatic inflammation—two hips, two knees, two ankles, two shoulders, two elbows, two wrists, two hands, and one heart, and the one functional characteristic common to the fibrous textures of all is that they are habitually engaged in controlling and regulating movement. They are the only fibrous textures which possess this function.

But though the fibrous structures and synovial membranes are the tissues on which the rheumatic poison produces the most marked effects, they are not the only ones which give evidence of disturbance. The evidence is most pronounced in them because the symptoms which constitute it—pain and swelling—are so prominent and obvious. So much do such symptoms force themselves upon the notice of both patient and physician, and so dominant are they during the whole course of the disease, that attention is naturally concentrated on them. But a careful consideration of all the phenomena which go to constitute an attack of acute rheumatism indicates that the muscles suffer at the same time as the joints. Their participation in the morbid process is indicated by the muscular pains and aching which usher in the attack, by the tenderness to touch of the muscles, and by the rapidity with which their tissue wastes away. Further very distinct evidence of disturbance of the muscles is found in what, next to fever and joint pains, is the most essential and characteristic feature of the disease—excessive formation of lactic acid. This phenomenon calls for explanation as urgently as the joint inflammation, for it forms as characteristic and as constant a feature of acute rheumatism; acid sweats are almost as essential to the diagnosis of acute rheumatism as joint pains.

Lactic acid is a normal product of the metabolism of muscle. In its quiescent state muscle gives a neutral or feebly alkaline reaction, when actively contracting the reaction is acid. This acid reaction is due to the presence of lactic acid formed during the state of activity.

Lactic acid being formed during muscle metabolism, excessive formation of that acid in the system indicates increased metabolism of muscle. As this excess of acid always occurs in acute rheumatism and never in any other disease, it follows that an increase in muscle metabolism is one of the characteristic features of the rheumatic process—one of the results of the action of the rheumatic poison. The consideration of the question of an excess of lactic acid in the system really resolves itself into the consideration of the question as to why muscle metabolism is increased. To this point we shall return by and by. Attention is called to it now with the object of showing that the rheumatic process is not limited to the white fibrous structures of the joints, but affects *all* their fibrous structures, the muscles as well as the tendons and ligaments.

The Nature of Rheumatism.

The nature of the change which takes place as the result of the action of the rheumatic poison has been the matter of some difference of opinion. The one point on which all are agreed is that it is inflammatory. The point on which opinions differ is as to the nature of the inflammation.

Rheumatic inflammation has been regarded by some as differing from ordinary inflammation, not essentially, but only in the peculiarity of its seat. By others it is looked upon as specific in nature, as resulting from the action of a special poison which does not operate in the production of other than rheumatic inflammation. The former is the view taken by those who regard the disease as the direct result of exposure to cold and damp; the latter that held by those who look upon it as due to the action of a special *materies morbi* circulating in the blood. That exposure to cold and damp suffices to produce acute rheumatism is an old view which finds its chief support in the fact that the disease often occurs after such exposure. But so frequent is such exposure that it would be difficult to point out any disease which might not be attributed to this agency, if we are not careful to distinguish between the *post* and *propter hoc*.

If acute rheumatism owned such a causation, it ought to be most common in the coldest climates, and during the coldest weather. But it is a disease of temperate climates, not of the arctic regions; and, in temperate climates, is not always most common in winter.

It ought, too, if caused by cold, to be most common in children and in old people, who have little power of resisting cold; but the reverse is the fact; for the disease is most common at the age at which the power of resisting cold is greatest—from fifteen to fifty. If

caused by exposure to cold, the joints which suffer most from such exposure, those of the fingers and toes, should also suffer most from rheumatism; but they are very rarely involved in the disease. Then again, if this be the cause of the disease, how is it that pericarditis so frequently occurs, and pleuritis and peritonitis so rarely? The pleura and peritoneum are just as much exposed to cold as the pericardium, probably more so. And how, on this view, are we to explain the occurrence of endocarditis, and the almost entire limitation of this to the left side of the heart?

Again, it is an established fact in the history of acute rheumatism that fresh joints may be attacked after the sufferer has been confined to bed in a warm room for days and even weeks. These later joint attacks are identical in nature with the earlier ones which ushered in the seizure, and it would be unreasonable not to regard them as produced in the same way, and as due to the operation of the same cause. But it is quite impossible that they can be caused by exposure to cold. The exclusion of cold as a possible cause in the case of these later joint seizures is a sufficient reason for calling in question its claims to be the cause of the earlier ones.

Other peculiarities of acute rheumatism there are which it is impossible to explain on this view of its etiology. The mere enumeration of these will suffice to show that no amount of exposure is adequate to their explanation.

The special characteristics of acute rheumatic inflammation are:

1. The tendency to its occurrence is hereditary—transmitted from father to son.

2. It is specially liable to occur at a particular age—being rare before fifteen or after fifty.

3. It is apt to attack the same individual again and again.

4. It does not confine itself to one joint, but affects several simultaneously or in succession.

5. It attacks also the membranes of the heart.

6. It very rarely terminates in suppuration.

7. It is not much benefited by measures calculated to relieve simple local inflammatory action, but is speedily subdued by proper constitutional treatment.

There is no possibility of explaining these peculiarities by any view which does not recognize the existence and operation of a generally acting internal cause. No external agency can be regarded as adequate to the explanation of any one of them.

1. The hereditary transmission of the rheumatic tendency necessarily involves the idea of a constitutional, not a local, malady. It means that a certain diathesis, or particular state of the body, pre-

disposing to rheumatism, is handed down from father to son. But such transmission can take place only in connection with constitutional ailments. We talk of a gouty, a rheumatic, a strumous, a cancerous diathesis; but never of a pleuritic, a peritonitic, or a nephritic one.

2. The tendency to attack those of a particular age is a feature which is noted specially in connection with diseases owning a constitutional origin; and which is manifested in rheumatism, as it is in struma, gout, cancer, etc.

3. The liability to repeated attacks in the same individual equally points to constitutional predisposition.

4. The fact that many joints suffer simultaneously or in succession, points to a generally operating internal and constitutional cause; for it is most improbable that an external and local cause could habitually produce inflammation in so many different parts as suffer during a rheumatic attack independently of a constitutional predisposition.

5. The tendency to heart affection can be explained only on the view that the true cause of the inflammation exists in the system. That cold and damp might give rise to an endo- or peri-carditis is possible; but that the occurrence of such inflammation in thirty-three per cent. of the cases of acute rheumatism can be due to other than a generally acting constitutional cause, is in the highest degree improbable.

6. The rarity of suppuration, no matter how intense and prolonged the inflammation, indicates that rheumatic is essentially different from ordinary inflammation. "I have often known acute rheumatism of the severest kind have the start of the remedy, full ten days or a fortnight, during which nothing whatever has been done for its relief; and when at length the remedy has been applied, it has been cured as easily and rapidly as I could promise myself that it would have been had I taken it in hand ten days or a fortnight sooner.

"Surely here is something remarkable enough to make us stop and think for a moment. An inflammation of the brain, the liver, or the lungs would not thus wait our pleasure, or our neglect, and be as curable ten days or a fortnight hence as it is to-day. For inflammation in these organs does not stand still. It is progressive from stage to stage, and each succeeding stage carries it further and further away from the remedy. But it is the very peculiarity of acute rheumatism that it *does*, in a certain sense, stand still. All its actions and movements are simply as forcible and rapid as possible, yet does it stand still. All its energy is expended upon one stage, and there is no apparent progression beyond it. A fortnight ago there was

great heat, and nervous and vascular excitement, and great pain and swelling of the joints; and, to-day, the heat, and nervous and vascular excitement, and pain and swelling are exactly of the same amount as they were at first. There is no more sign of parts disorganized, or parts destroyed, now than then" (Latham).

7. Finally, the success of constitutional, and the futility of local, treatment complete the proof that in rheumatism we have to deal with an ailment which owns an internal and constitutional, and not an external and local, cause.

But though exposure to cold and wet are not *per se* the cause of acute rheumatism, there is ample evidence, the result of the accumulated experience of all countries and all observers, that such exposure often acts the part of an aider and abettor in determining a rheumatic attack. It does not itself give rise to the disease, but it renders the systems of those liable to be affected by the special cause of acute rheumatism more susceptible to its action.

How it does so is one of the questions which have to be considered in connection with the different theories advanced as to the nature and mode of action of this special cause.

Theories of Rheumatism.

The Lactic-Acid Theory.

Blood poisons may be divided into two classes: (*a*) Those which are produced within the system; and (*b*) those which enter it from without. The rheumatic poison is generally regarded as belonging to the former—as being some product of mal-assimilation, or imperfect tissue metamorphosis.

One of the characteristics of acute rheumatism is the occurrence of profuse acid perspirations. The urine too is hyperacid. This excessive acidity naturally led to the hypothesis that an acid condition of the blood had something to do with the production of the rheumatic symptoms. Dr. Prout made the definite suggestion that the *materies morbi* was lactic acid, and that the rheumatic symptoms resulted from the accumulation of this acid in the blood. This idea, enlarged upon and developed by Todd, Fuller, and others, was regarded by the profession as affording of the causation of acute rheumatism a more satisfactory explanation than any other hypothesis hitherto advanced. It possessed, moreover, the advantage of affording a definite foundation for a rational line of treatment—the treatment by alkalies.

The lactic-acid theory was, for these reasons, very generally accepted, and for a long time was looked upon as quite satisfactory.

In time, however, the sufficiency of this theory began to be called in question, and doubts expressed as to the efficacy of the treatment by alkalies to which it naturally led. The failure of the alkaline treatment indeed, more than any other cause, tended to bring discredit on the acid theory.

Lactic acid is a product of tissue metamorphosis. It is an unstable compound, which readily undergoes change, and is excreted by the lungs and skin as carbonic acid and water.

Its presence in excess in the system may be due to increased formation, to defective elimination, or to a combination of these two agencies. The most perfect development of the lactic-acid theory is that which recognizes this combination.

Lactic acid is formed during the metabolic changes which take place in muscle. During exercise it is formed in larger quantity than during quiescence, and when the exercise ceases there is an excess of this acid in the system. But the exercise which causes increased formation of lactic acid is accompanied also by increased action of the lungs and of the skin, the channels by which the acid is eliminated in the form of carbonic acid and water. Excessive formation is thus counterbalanced by increased elimination, and no accumulation takes place. But if, at this time, the action of the skin be checked, the metamorphosis and elimination of the lactic acid are arrested, it accumulates in the system, and the symptoms of acute rheumatism result. The action of the skin is checked by anything which chills the surface of the body.

Such is the most perfect development of the lactic-acid theory; and such the manner in which this modern theory is combined with the old view as to the efficacy of a chill in the production of rheumatism. The theory is ingenious and beautiful, and by no means devoid of foundation. But it must not be accepted without a careful consideration of the evidence on which it rests.

The arguments adduced in support of this theory are the following:

1. Acute rheumatism is accompanied by excess of lactic acid in the system; the disease never occurs without such excess, and such excess is found only in connection with it.

2. The injection of lactic acid into the system of the lower animals has been said to be followed by inflammatory changes similar to those which occur in acute rheumatism.

3. The administration of lactic acid to man has been followed by symptoms indistinguishable from those of acute rheumatism.

Let us consider each of these arguments.

1. *Acute rheumatism is accompanied by excess of lactic acid in the system, and such excess is noted only in connection with it.*

That no doubt is true; and the accuracy of the statement is not called in question. The point at issue is the relationship which this excess of acid bears to the rheumatic process. Is lactic acid the rheumatic poison, and does its presence in excess in the system give rise to the phenomena of acute rheumatism; or is the excess of lactic acid, like pain and fever, merely one of the phenomena of the disease, one of the results of a morbid action set agoing by some other agency?

According to the lactic-acid theory, the acid causes the rheumatism. The main support of this theory is the fact which we are now considering, that there is always an excess of lactic acid in the system during the course of acute rheumatism.

But there are cogent reasons for not accepting the view that the acid is the cause of the rheumatism. For if it were so, the rheumatic symptoms should persist so long as the acid existed in adequate excess in the system, and should decline when it ceased to do so, and not till then. Remedies, too, which neutralize the acid should also cure the rheumatism; while those which did not do so should fail to have any curative effect. The early advocates of the lactic-acid theory believed that the administration of alkalies, by neutralizing the acid, would cure the rheumatism. And theoretically such should have been the case. But the reality has been very different. For though, in the absence of any better mode of treatment, alkalies continued to be for many years the chief remedies administered in rheumatism, we very well know that they exercise little or no control over the disease. They may be given so as to saturate the system, and render the urine alkaline, without doing good to the rheumatism. The disease seems to last as long, and to run the same course when treated by alkalies, as it does when it receives no treatment at all. If the acid caused the rheumatism this should not be.

Again, we find that salicin and salicylic acid cure acute rheumatism effectually and speedily—as will be evidenced further on. It is impossible that their curative effect can be due to any neutralizing action on lactic acid. Their effect is produced also independently of any action on the eliminating organs. It is certain that these remedies neither neutralize nor get rid of the acid, for in cases of acute rheumatism which are thus cured the perspiration often continues to give an acid reaction for four, six, or more days after fever, pain, swelling, and all symptoms of rheumatism, except this acidity, have disappeared. This continued acidity of the perspiration so long after the rheumatic symptoms have ceased is no doubt due to the presence and excretion of acid formed during the continuance of the disease. It has an important bearing on its pathology.

It indicates, first, that the acid in the system is neither neutralized

nor destroyed by the remedy which neutralizes the action of the rheumatic poison, arrests the rheumatic process, and puts an end to the disease.

Secondly, it shows that the mere presence of lactic acid in the system does not necessarily give rise to rheumatic symptoms.

Thirdly, it indicates that it is the *production* of the acid in excess, not its mere *presence* in excess, which is essentially associated with these symptoms. In other words, these symptoms and the presence of lactic acid in the system would seem to be associated together as conjoint results of the rheumatic process. On this view of the matter excess of lactic acid in the system becomes one of the ordinary symptoms of acute rheumatism—a result and not the cause of the morbid process which constitutes the disease.

2. *The injection of lactic acid into the systems of the lower animals has been said to be followed by inflammatory changes similar to those which occur in acute rheumatism.*

Many years ago Sir Benjamin Ward Richardson published an account of some experiments made on cats and dogs, by injecting lactic acid into their peritoneal cavities. The results of these experiments he regarded as favorable to the lactic-acid theory of rheumatism; and they have been referred to by various authors as one of the reasons for accepting that theory.

A careful perusal of Dr. Richardson's paper would seem to indicate that there have been accorded to his experiments a wider scope and greater significance than are their due. For in none of the animals experimented on was there induced a morbid condition which we would call rheumatism in man. What Dr. Richardson found, and all that he found, was that in animals into whose system lactic acid had been injected, there was observed, after death, redness of a portion of the endocardium. Endocarditis, and not rheumatism, seemed to be the malady induced. But as endocarditis is frequent, and an excess of lactic acid invariable, in acute rheumatism, the inference was drawn that these experiments demonstrated the accuracy of the view that lactic acid is the morbid agency which gives rise, not only to endocarditis, but also to the rheumatism with which endocarditis is usually associated. The inference is wider than the facts warrant.

Moreover, a careful examination of these facts indicates very important points of difference between the condition noted by Richardson and that which occurs in connection with acute rheumatism—so important, that we are led to regard the results of his experiments as negative, so far as the pathology of acute rheumatism is concerned, and the inferences drawn from them as inadmissible.

What Dr. Richardson teaches is that in both induced and rheu-

matic endocarditis the cause of the inflammation is lactic acid in the blood, and that the acid produces its effect by a direct irritant action on the free surface of the endocardium.

The bearing of his experiments on our subject may be considered under the following propositions, taken from Dr. Richardson's paper, and given in his own words:

1. "In rheumatic endocarditis the poison is produced in the pulmonary and destroyed in the systemic circulation."

2. "Lactic acid could not exist in the blood without producing endocardial mischief."

3. "The action of the poison which produces the disease (rheumatic endocarditis) is directly on the free surface of the endocardial membrane; the poison acts, in a word, after the manner of a local irritant."

(*a*) The first proposition is a most important one—so important that it cannot be accepted without evidence; for on its accuracy depends the validity of Dr. Richardson's whole argument.

If his statement be correct the fact which it indicates strongly supports his view of the mode of production of endocarditis.

If, on the other hand, it can be shown that lactic acid, so far from being destroyed, is actually produced in the systemic circulation, then Dr. Richardson's statement is proved to be erroneous, and his position untenable. A careful study of the question would indicate that such evidence does exist.

During the process of digestion sugar is formed. From the digestive organs it passes into the circulation. Part of it is taken up by the liver, and converted in that organ into glycogen, in which form it is stored up in the liver. During fasting it again becomes transformed into sugar, and as such passes into the circulation. Like all non-nitrogenous substances, sugar is finally transformed into carbonic acid and water. In the course of this transformation there are produced various intermediate substances. One of these is lactic acid. The question which we have to consider is, where does this formation of lactic acid take place? Our knowledge on this point has considerably advanced since Richardson made his experiments; and it is now known that lactic (sarcolactic) acid is one of the metabolic products of muscle. In the passive state muscle has a feebly alkaline reaction; but during contraction it becomes acid. This altered reaction is of course due to the formation of an acid in the muscle; and du Bois-Reymond showed that the acid formed is sarcolactic acid. His observations were confirmed by those of Heidenhain, who found that up to a certain point the quantity of acid produced increased with the amount of work done by the muscle. It has been

maintained by some that the acid reaction of the active muscle is partly due to the formation of phosphoric acid. Be this as it may, there can be no doubt from the observation of du Bois-Reymond that it is at least partly due to the presence of sarcolactic acid, and that that acid is a metabolic product of muscle and is formed during its contraction. Richardson's statement that the acid is formed in the pulmonary and destroyed in the systemic circulation is thus demonstrated to be erroneous.

(*b*) The second proposition, that lactic acid could not exist in the blood without producing endocarditis, is equally at variance with facts and experience.

"It is absurd," says Richardson, "to assume that ounces of an acid of the producing series thrown off from the skin of a sick man should not be derived from his blood." Lactic acid is thus thrown off from the skin in acute rheumatism. If Dr. Richardson's proposition were correct, endocarditis should be an invariable complication of that disease. But it occurs only in a minority of cases, about 30 per cent. Lactic acid, therefore, exists in excess in the blood, without producing endocardial mischief, in about 70 per cent. of the cases of acute rheumatism which occur.

(*c*) The third proposition, that lactic acid acts as a local irritant to the endocardium, is in keeping with the second; but is equally inconsistent with evidence, and is refuted by the same arguments. If lactic acid be the rheumatic poison, and if it exercise a direct irritant action on the endocardium, that membrane should give evidence of irritation in every case of acute rheumatism; but it does so in only a minority. Again, if this were its mode of production the inflammation should be diffused over the whole surface of the endocardium; but it is limited to the valves, and even in these is found only on one side—in the aortic valve only on its convex surface, and in the mitral only on its auricular.

The pathogenesis of rheumatic endocarditis ought not to, and cannot rightly, be considered apart from that of the joint inflammation in connection with which it occurs. The poison which gives rise to the one gives rise to the other; and its mode of action in the production of inflammation of the fibrous and serous tissues of the joints and of the heart, is doubtless the same. It is physically impossible for lactic acid to act on the fibrous elements of the joints, as Dr. Richardson believes that it acts on the endocardium.

Again, pericarditis is almost as frequent as endocarditis in acute rheumatism. The two are due to the same cause, and produced in the same way; but Dr. Richardson leaves pericarditis out of account altogether, and gives of the occurrence of inflammation of the mem-

brane which lines the interior of the heart, an explanation which cannot apply to inflammation of that which invests it externally.

For these various reasons, we regard the inferences which have been drawn from Dr. Richardson's experiments as fallacious and unwarranted; and the experiments themselves as affording no valid support to the lactic-acid theory of rheumatism. The results of experiments made on the lower animals may readily have their importance exaggerated; and we cannot exercise too great caution in drawing from them inferences applicable to man. Though certain effects are got from the administration of this and that drug to a cat or dog, it by no means follows that like results would follow its administration to man. This objection is peculiarly applicable to Dr. Richardson's experiments. There are abundant observations to show that the only invariable result of the administration of lactic acid to man is increased action of the skin. But this is a result which could not be got in dogs, for they do not perspire.

But above and beyond all these very cogent reasons for rejecting Dr. Richardson's teaching there is another one even more potent. It has been demonstrated by Reyher that the endocardial signs which Dr. Richardson attributed to the action of lactic acid are found in all dogs, no matter how they are killed. Richardson, and Rauch who supported him, omitted to satisfy themselves before making their experiments as to what was the normal appearance of the endocardium in the dog after death. Had they done so they would have found it to be exactly that which they described as morbid, and as the result of the action of lactic acid on it. The redness which Richardson regarded as pathological, and as the result of the direct irritant action of the lactic acid, has been shown to be the normal condition of the lining membrane of the right side of the heart of the dog, no matter how death is brought about.

3. *The administration of lactic acid to man has been followed by symptoms of acute rheumatism.*

Since Cantani recommended lactic acid as a remedy in diabetes, numerous cases of that disease have been thus treated. In several the administration of the acid has been followed by symptoms indistinguishable from those of rheumatism, pain, and swelling of joints, with rise of temperature.

One of the most remarkable is a case related by Dr. B. Foster in which there occurred six well-marked arthritic attacks: "The phenomena corresponded in all respects to those which are characteristic of acute articular rheumatism. They came on when the acid was taken, and ceased when it was discontinued. When moderate quantities of the acid were tolerated, an increase in the dose was succeeded

by the painful inflammation of the joints. Coinciding with the development of the articular affection was the appearance of perspiration, at first only slight, but afterward, in the more severe attacks, copious and acid. These facts," continued Dr. Foster, "have dispelled the last lingering doubt in my mind as to the truth of the lactic-acid theory of rheumatism."

One cannot read the details of Dr. Foster's cases without feeling that we have in their facts strong evidence in support of the lactic-acid theory—to my mind, the strongest that has been adduced in its favor. Such evidence cannot be disregarded or ignored; either we must explain it, or our refutation of the lactic-acid theory must remain imperfect and inadequate. Can it be explained? I think it can; and that even Dr. Foster may be shaken in his renewed allegiance to his old love.

Lactic acid is a product of tissue metabolism—an excretory product therefore. Such products when retained unduly in the system exercise two distinct actions—first, a stimulant action on the organ by which they are normally eliminated, and second, a disturbing action on the tissues which supply the materials from which they are formed. The retention, for instance, of an excess of carbonic acid in the system causes, first, increased force and frequency of respiration, and ultimately paralysis of that function and asphyxia. Excess of urea in the blood causes, first, increased action of the kidneys, and ultimately that condition of tissue asphyxiation to which we apply the term uræmia. So with lactic acid, its retention in the system causes, first, increased action of the organ by which it and its products are normally eliminated, and second, functional disturbance of the textures during whose retrograde metamorphosis it is formed, if for any reason the eliminating organ failed in its duty.

Observation has shown, first, that lactic acid is eliminated chiefly by the skin, and second, that it is formed during the action and retrograde metamorphosis of the tissues of the motor apparatus. The effects which we should expect to result from an excess of lactic acid in the blood, are, therefore, increased action of the skin, and, failing that, functional disturbance of the motor apparatus. And that is exactly what Dr. Foster observed.

Lactic acid is so readily oxidized and eliminated, that it is only in exceptional cases that ingestion can exceed elimination. Hence it is only in exceptional cases that its internal administration can give rise to disturbance. One of these exceptional cases is that recorded by Dr. Foster. The patient was suffering from diabetes and phthisis—both of them ailments accompanied by imperfect oxidation. "In diabetes," says Dr. Foster, "we have a state of disordered nutrition

very unfavorable to the conversion by oxidation of new compounds; and in Wright's case this was aggravated by the serious pulmonary complications. Associated with this was a dry branny state of the skin highly unfavorable to the elimination of the lactic acid by one of the common channels."

Lactic acid given under such circumstances—given, that is, to a man in whose system it cannot be oxidized, and by whose skin it cannot be eliminated—must be retained, and cause disturbance of the nutrition of the textures of whose metamorphosis it is a product. An excess of lactic acid in the blood checks the retrograde metamorphosis of these textures, and so disturbs their whole nutrition, just as retained excreta produce a corresponding action on the brain, and as an atmosphere of carbonic acid interferes with the elimination of that gas from the system. The symptoms resulting from the retention of lactic acid in the blood are, therefore, likely to be those of functional disturbance of the tissues of the motor apparatus. Functional disturbance declares itself in different ways in different organs. In the brain it causes nervousness, irritability, headache, giddiness, delirium, convulsions, and coma. In the heart it gives rise to more or less disturbance of the rhythm and force of its action. In the digestive organs it declares itself by evidences of imperfect and deranged digestion. In fibrous tissue the evidence of its existence is pain, which may be very severe, and is well exemplified by what is felt when a ligament is unduly stretched, or when, as in acute rheumatism, it is the seat of inflammation.

A disturbing agency like lactic acid, which acts on both the muscular and fibrous textures, will declare itself chiefly by symptoms referable to the latter. It will do so, because these textures give more ready and decided evidence of functional disturbance; and because any weakening of the muscles to which it might give rise would be lost in the muscular debility and wasting characteristic of the diabetes for which the acid was given.

Pain localized in the muscular and fibrous tissue of the motor apparatus is, therefore, the chief symptom which we should expect to find follow the retention in the blood of an excess of lactic acid. And so in reality it is found to be. That is the true interpretation of Dr. Foster's facts. His evidence shows that lactic acid causes increased action of the skin; and failing this, disturbed nutrition of, and consequent pain in, the muscles, and in the fibrous textures of the joints; but it goes no further.

But it may be said, if you grant this—if you admit that excess of lactic acid in the blood may give rise to articular pains—do you not thereby admit the truth of the lactic-acid theory of rheumatism? By

no means; the two propositions are not only not identical, but are widely different. That excess of lactic acid in the blood is the cause of some of the phenomena of acute rheumatism, is a position which I not only admit, but am prepared to maintain. But that is a very different thing from saying that it causes all its phenomena, which is what the lactic-acid theory asserts. That theory is, that lactic acid is *the rheumatic poison*, the special *materies morbi* which initiates and sets agoing all the phenomena of the disease. One of the most constant of these phenomena is the presence in the blood of an excess of lactic acid. But lactic acid cannot be the cause of its own increased formation—of its own excess. The position is an absurd one; but its very absurdity serves to demonstrate the weakness of the lactic-acid theory, and to bring before us the real nature of the question which we have to consider, and of the difficulties which we have to face.

The advocates of the lactic-acid theory of rheumatism have taken one of the phenomena of the disease, and have raised it from its normal and subordinate position of a symptom, to the rank and dignity of an exciting cause. In so doing they have necessarily fallen into error. Excess of acid may cause joint pains, but what causes the excess of acid? That has to be explained, no less than the phenomena which combine with it to form the symptoms of acute rheumatism.

And herein we see the inadequacy of Dr. Foster's observations to throw light on the ultimate pathology of the disease; and the short-sightedness of the view which regards them as doing so. In his cases the lactic acid was given to the patient, and its presence in excess was readily accounted for. In acute rheumatism the excess of lactic acid is the phenomenon which, of all others, it is at once most essential and most difficult to explain. If the first requisite to the production of rheumatism be an excess of lactic acid, the first requisite to a satisfactory theory of rheumatism is that it should account for this excess. An attempt to do so has been made by some of the advocates of the lactic-acid theory, notably by Corrigan and Senator. Lactic acid, they say, is formed during muscular exercise. Under ordinary circumstances it is partly oxidized and got rid of as carbonic acid and water; partly, when there is a great deal of it, excreted unaltered in the sweat. Should the cutaneous surface be chilled, the elimination of the acid will be checked, and it will accumulate in the system.

That chilling of the surface when heated by exercise may be followed by a rheumatic attack there is no doubt. But to be heated by exercise is so common at the age at which acute rheumatism chiefly occurs, and to be exposed to cold so common in the climate in which

it most prevails, that great allowance has to be made for the elements of chance and accidental coincidence. But making allowance for these, there can be no doubt that overheating and subsequent exposure to cold, and even such exposure without previous overheating, do in some cases seem to determine a rheumatic attack. But it does not follow that the determining agent is the checking of the action of the skin. Overheating and subsequent chilling are not the only effects of exercise and subsequent exposure; they are not even the most common. A more constant and more important one is exhaustion, and the probable explanation of the connection which obtains between the exercise and the rheumatism is that the exhaustion consequent on the exercise renders the system more susceptible to the action of the rheumatic poison. The depressing influence of cold by lowering the whole vitality would lead to the same result.

A greater liability to the action of certain morbific agencies, when the system is exhausted or depressed from any cause, has been noted in connection with many diseases. Referring to malarial fevers, with which, as we shall by and by see, rheumatic fever has many analogies, Niemeyer says: "Exhausting exercises and other debilitating influences, errors of diet, and particularly catching cold, increase the predisposition so much, that persons who have long been exposed to malaria with impunity are not affected by it till one of these causes has acted on them."

In the case of acute rheumatism it is not so much the exercise as the exhaustion which follows it; it is not so much the chilling of the surface as the depressing action of the cold on the system which are the disturbing agencies. They do not themselves produce the disease, but they render the system more liable to the action of the rheumatic poison.

There are other cogent reasons for rejecting the view that chilling of the surface plays the part attributed to it in the production of acute rheumatism. In the first place, it is to be noted that chilling of the surface when heated by exercise is frequently had recourse to with impunity, if not with actual benefit. Then again, if we regard sudden chilling of the surface as a danger, and as a cause of acute rheumatism, how are we to explain the beneficial action of the cold bath in the hyperpyrexia of malignant cases of that disease? Here we have the malady presenting itself in the most distinct form, lactic acid is being freely thrown off by the skin, the patient is in imminent danger, and yet the only thing which does him good—the only thing which seems to give him a chance of recovering—is to apply cold to the surface, thereby not only lowering the temperature, but checking also the action of the skin. The same agency which is blamed for

causing the patient's illness is applied in a more decided manner to get him out of it, and is really the only reliable means of attaining this end.

This theory as to the mode of production of acute rheumatism, and of the operation of cold, has other inherent weaknesses.

It means, first, that during half-an-hour's violent exercise there is formed in the systems of those of rheumatic constitution enough lactic acid to produce an attack of acute rheumatism; second, that every time they take active exercise, such persons are liable to be laid up by that disease; and, third, that they are saved from such a misfortune only by the free action of their skins. Nature often bungles, but never to that extent.

But still more is involved in this belief; for, if we adopt it, we must also believe that during half-an-hour's violent exercise there is produced in the system enough lactic acid not only to give rise to acute rheumatism, but to keep up the symptoms of that disease for weeks, and to supply at the same time the excess of acid which is being eliminated during the whole period of the continuance of the malady. The mere statement of what is involved in this belief suffices to condemn it. For to suppose that the whole of the lactic acid which is required to produce an attack of acute rheumatism of several weeks' duration, with its accompanying profuse acid perspirations, could be produced in the system in the course of half an hour, is to presuppose the existence in the system, at the end of that half-hour, of a quantity of lactic acid, which (granting that acid to be the cause of the rheumatism) would produce the most acute inflammation of all the tissues of the body liable to rheumatic inflammation, and kill the patient by such inflammation in two or three days. On this view of its causation and nature all cases would be acute, and the disease would be more formidable and fatal than it is.

Again, if the poison of the disease were thus produced—if the whole of the *materies morbi* existed in the system at the commencement of the attack—which would be the case if the above view were correct—we should find the symptoms of acute rheumatism developed, not gradually as is the case, but quickly, and very soon after the chill was applied; we should have the joints affected, not in succession as is the case, but all at the same time, and also very soon after the chill; and we should have the heart involved in every case. We should find, too, that the free action of the skin, and consequent elimination of the acid, which characterize the disease, would be followed by relief of the pain; and that we know is not the case.

No, it is simply impossible that the gradual onset of the symptoms of acute rheumatism, the protracted and varying course of the

disease, the shifting character of the joint inflammation, and the long-continued hyperacidity of the secretions, can result from such an excess of lactic acid as could be produced in one or in a dozen hours' violent exercise. In an attack of acute rheumatism there is eliminated by the skin alone in twenty-four hours a quantity of acid greater than is likely to exist in the system at the end of an hour's exercise.

It is erroneous and misleading to regard the excess of lactic acid, which undoubtedly does exist in acute rheumatism, as simply an accumulation. The use of this term, and the undue importance attached to the operation of cold, have led to a misinterpretation of the phenomena observed. What we mean when we say that an excretory product accumulates in the system, is that it is being formed but not properly eliminated. But in acute rheumatism there is increased, and very greatly increased, elimination as well as increased formation; and this increased elimination goes on during the whole course of the malady. The most severe cases, those in which there is most suffering, and most of the characteristic joint affection, are also those in which the perspiration is most profuse and most markedly acid, and in which, therefore, the acid is most freely eliminated. We cannot say that in such circumstances there is any accumulation of lactic acid in the system; for it is being eliminated in unusual quantity. Such increased elimination implies, not accumulation, but increased formation; and *this* is the phenomenon which calls for attention and for explanation. Increased formation of lactic acid is one of the essential features of acute rheumatism; and no theory of that disease can be regarded as satisfactory, which does not recognize and account for this increase. This the lactic-acid theory fails to do.

Other symptoms of the disease, too, this theory not only does not explain, but does not even take cognizance of. In advancing a theory of the causation of acute rheumatism, we have to account, not only for the occurrence of the joint pains, the febrile disturbance, and the acid sweats, but for the occurrence of the symptoms which precede these special and characteristic manifestations of the fully developed disease; and precede even the evidence of the existence of an excess of lactic acid. A case of acute rheumatism does not leap at once *in medias res*. The characteristic symptoms of the disease are preceded often for two, three, or more days by shivering, *malaise*, and a sense of weakness accompanied by aching of the limbs. These initial symptoms are as much a part of the ailment as the joint pains which they usher in, and have equally to be accounted for. This the lactic-acid theory does not even attempt to do.

But while we reject the view which regards lactic acid as the cause of rheumatic fever, as the morbific agency which originates the

disease, we are far from regarding that acid as without action, and as having no share in the production of the phenomena of a rheumatic attack. An excess in the blood of any product of retrograde tissue metamorphosis could scarcely be without some action. And there can be no reasonable doubt that the profuse perspirations which form a characteristic feature of the disease are mainly due to the stimulant action on the skin of the excess of lactic acid in the blood. It is probable, too, that should formation exceed elimination, the resulting excess of acid would tend to exaggerate the already existing disturbance of the fibrous tissues, and so aggravate the pains and general symptoms of the malady.

We shall by and by see that there is reason to suppose that cases in which the fibrous tissues have been weakened and rendered irritable by frequently repeated rheumatic attacks may have their convalescence retarded and the ailment prolonged by the action of the acid on the altered fibrous tissues. Such cases may be placed in the same category as that related by Dr. Foster. They tend to show that the presence of an excess of lactic acid in the blood has a disturbing action on the fibrous tissues; but they do not show that that acid is the rheumatic poison.

The Neurotic Theory of Rheumatism.

One of the most prominent and popular of modern physiological doctrines is that which teaches that every physiological act and every normal function is carried on under the controlling influence of the nervous centres.

A doctrine at once so simple and so far-reaching could not fail to strike pathologists, and to be applied by them to the explanation of some of the phenomena with which they have to deal. If such and such a function is dominated by a special nervous centre, and is dependent for its due performance on the integrity of that centre, may not the derangements of that function which are noted in disease be the result of disturbances originating in its dominating centre? The general doctrine thus formulated evidently admits of wide application. Theoretically there is scarcely any disorder of function to which it might not be applied with some degree of plausibility; and there is considerable danger of our being seduced into the too free utilization of so simple a doctrine in explanation of morbid phenomena. Against this danger we must be on our guard.

An instance of the ready appropriation of this doctrine by pathologists we have in one of the modern views as to the causation of pyrexia. Physiology teaches that the nervous centres exercise a con-

trolling influence over the heat of the body; and clinical research has demonstrated that some injuries and non-inflammatory lesions of the nervous centres cause a rise in the temperature of the body. The increased body heat noted in such cases is clearly of neurotic origin, and the demonstration of the occurrence of such rises of temperature naturally suggests a neurotic theory of fever. But the application of this theory to the explanation of the occurrence of all forms of fever is an instance of the too free application of the doctrine in question. Because in some cases increased body heat is of neurotic origin, it does not follow that all fever is so. The inference is wider than the facts warrant.

Another example of the free application of the doctrine to the explanation of the phenomena of disease—that which specially concerns us at present—we have in the attempt to explain by it the occurrence of rheumatic inflammation of the joints.

It is an established fact in pathology that joint troubles occur as a sequence of lesions of nerves and nerve centres. Charcot, describing them as they occur in connection with brain lesions, says that they are chiefly found in cases of hemiplegia where the paralysis is consequent on encephalitis or brain-softening. Brown-Séquard, referring to the pain sometimes experienced when paralyzed limbs are pressed upon or moved, says that such pains "depend upon a subacute inflammation of the muscles or joints which is often mistaken for a rheumatic affection." Dr. J. R. Mitchell as far back as 1831 called attention to joint changes occurring as a sequence of injuries of the spine. More recently attention has been prominently directed to this subject by his son, Dr. Weir Mitchell, who describes the "curious inflammatory states of the joints" which follow injuries to nerves, especially those of the arm. Then again, as research has advanced and knowledge increased it has become more and more certain that rheumatoid arthritis is a disease *per se*, quite distinct from both gout and rheumatism both in its clinical history and in its pathology; and the special attention which as a separate ailment it has received has led pathologists more and more to lean to the view originally advanced by Remak, that the joint changes which form its characteristic feature are somehow or other the result of malnutrition consequent on weakening of nerve centres.

With the growing belief in the doctrine of the localization of cerebral function, and of the part played by nerve centres in controlling and regulating the functions of organic life; with such distinct evidence as we have that serious joint changes do take place as a consequence of lesions of nerves and nerve centres, and with the mind of the profession all but made up that rheumatoid arthritis is of neurotic origin,

it was inevitable that we should ere long hear of a neurotic theory of rheumatism. Such a theory was indeed suggested by the elder Dr. Mitchell, but the suggestion lay dormant till increasing knowledge of the subject to which he drew attention, the occurrence of joint troubles as a sequence of nerve lesions, combined with the result of the separate study of the pathology of rheumatoid arthritis, led to its revival.

This theory has assumed two forms.

By most of those who advocate it the disturbance of the nerve centres which originates the joint troubles is believed to be produced by peripheral irritation applied to the surface nerves, and transmitted by them to the nutrition centres of the joints. That joint troubles might thus be induced there can be no doubt; but that acute rheumatism could be so caused seems to me highly improbable. For in the first place acute inflammation such as that which characterizes the joint affection of that disease is not the form of joint trouble which we find associated with lesions of nerves and nerve centres. Nor can it be regarded as *a priori* other than highly improbable that such acute sthenic inflammation should be the result of malnutrition. And, in the second place, inflammation of the joints is not the only thing with which we have to deal in acute rheumatism. The disease has other features and other phenomena calling for explanation as much as do the joint lesions. If, for instance, as is maintained, cold be the common cause of the peripheral nerve irritation which sets the malady agoing, why is the disease more common in temperate than in cold climates? Why is it most common at the age at which the power of resisting cold is greatest, fifteen to fifty? And why so rare among children and older people whose power of resisting cold is so much less? Again, how on this view are we to explain the invasion of fresh joints after the patient has been warm in bed for days, maybe for weeks? How account for the occurrence of endocarditis and pericarditis? Why is the endocarditis so limited in extent? Why does it affect only the valves of the left side, and only one surface of the valve? How account for the excess of lactic acid in the system?

These are all points of which an explanation must be given; and no theory of rheumatism can be regarded as satisfactory which does not do so. But the neurotic theory takes no cognizance of the heart trouble, and offers of the joint inflammation an explanation which fails to deal with some of the characteristic features of that lesion.

The fact is that the phenomena of acute rheumatism are such as can be explained on no view which does not recognize the action of a poison which is produced in the system during the course of the

malady and circulates in the blood. Recognizing this, Dr. Latham, one of the most strenuous advocates of the neurotic theory, advanced the view that as a result of exposure to cold there is produced a hyperæmic state of the muscles, that from this there results an increased formation of glycocin, that this is ultimately transformed in the liver into uric acid, and that this uric acid it is which by impairing the action of the nutrition centres of the joints causes the inflammation noted in acute rheumatism. According to this view uric acid with some aid from lactic acid causes rheumatism much as it causes gout.

The objections to this very ingenious theory are, first, all those which have been already advanced against the original form of the neurotic theory—and, second, the fact which has been demonstrated by Garrod and others over and over again, that uric acid does not exist in excess in the blood in acute rheumatism. It is an acid which when it exists is very easily detected. According to Dr. Latham's hypothesis it ought to be there; but it really is not.

It may be laid down as a general rule in science that when we have to advance several hypotheses to explain one set of phenomena we are almost certainly on the wrong tack. Dr. Latham's theory of the mode of production of acute rheumatism bristles with hypotheses. The ability with which he manipulates them does not remove the weakness and inherent improbability imparted to his theory by their number, and the absence of facts to support them.

Of all acute febrile ailments acute rheumatism is the one in which the nervous centres give least evidence of disturbance. In typhus and typhoid fevers, scarlet fever, pneumonia, etc., there are generally symptoms distinctly and directly referable to disturbance of the brain. In rheumatic fever such symptoms seldom occur except in cases of hyperpyrexia and in cases complicated with acute carditis or pericarditis, and in them the nervous symptoms are due to special causes, and have no connection with the joint troubles.

Neither the natural history nor the clinical features of acute rheumatism support the view that the disease is of neurotic origin. As Arnozan remarks, "Avant de prononcer que les lésions articulaires du rhumatisme sont des lésions trophiques dépendant de la moëlle, il faudrait démontrer d'abord que celle-ci est réellement atteinte."

Pathological analogies have been inferred between gout, rheumatism, rheumatoid arthritis, and spurious arthritis because the joints are affected in each; but the analogies are really clinical, and we must be careful to distinguish between clinical and pathological analogy, or we shall fall into pathological error.

The joint troubles referred to represent four different ailments as

distinct in their pathological histories as are pneumonia, bronchitis, asthma, and pulmonary emphysema. Because these ailments consist each in some form of pulmonary trouble we do not infer pathological analogies between them, or refer each to disorder of the respiratory centre. Though we look upon asthma as a disease of the nervous system, we do not say that bronchitis is so too. During an attack of either ailment the calibre of the bronchial tubes is diminished, and their functional utility interfered with, but we do not allow such clinical analogies to blind us to the fact that the two ailments have no pathological affinity. The joint troubles which result from nerve lesions bear to acute rheumatism no closer resemblance either clinically or pathologically than asthma does to acute bronchitis; and a careful consideration of all the evidence leads us to indorse Arnozan's conclusion that "les rapports entre le système nerveux et le rhumatisme articulaire sont encore à trouver."

The Miasmatic Theory of Rheumatism.

In rejecting the neurotic theory of rheumatism we reject the view that the disease is due to disturbance originating independently of a special poison.

In rejecting the lactic-acid theory we reject the view that the rheumatic poison is generated within the system.

The only alternative view is that this poison enters the system from without.

Of such poisons there are two kinds—the contagia and the miasmata. What knowledge we possess regarding the nature and mode of action of these poisons has been got less from a study of the poisons themselves than from a study of the phenomena to which they give rise.

The essential properties of the fevers to which the contagia give rise are as follows:

1. They are communicable from the sick to the healthy.
2. They have a fixed and definite period of duration.
3. One attack, as a rule, confers immunity from a second.

But rheumatic fever is not communicable from the sick to the healthy; it has no fixed period of duration; and one attack confers no immunity against a second. As rheumatic fever bears no analogy to the contagious fevers its poison cannot be regarded as a contagium.

In studying malarial fevers the facts which force themselves most prominently on our attention are as follows:

1. They are most apt to occur in low-lying, damp localities, in certain climates, and at certain seasons of the year.

2. Some people are more liable to be attacked than others.

3. They have no definite period of duration.

4. They are not communicable from the sick to the healthy.

Now we cannot fail to see that these are quite the attributes of acute rheumatism. It is most common in temperate climates, at certain seasons, and in damp, low-lying localities; it has no fixed period of duration; it is not communicable from the sick to the healthy; some people are more liable to suffer than others; and its poison, we have seen reason to believe, enters the system from without. But the analogy between rheumatic fever and the common malarial fevers does not end here. A still further analogy may be traced in their clinical histories.

1. Malarial fever is irregular in type, and characterized by variations in its course. So is rheumatic fever.

2. Profuse perspirations characterize the course of malarial fevers; so they do that of rheumatic fever.

3. During the course of malarial fevers the urine is loaded with urates; so it is in rheumatic fever.

4. One attack of malarial fever seems to render the system more liable to its recurrence; the same is true of rheumatic fever.

5. Malarial fevers often leave an impress on the system which renders the sufferer liable to disturbance and the recurrence of some of their symptoms from slight causes. Rheumatic fever often has the same effect.

6. Unless arrested by treatment malarial fevers are apt to have a protracted and uncertain course; so is rheumatic fever.

7. The course of malarial fever is speedily arrested by large doses of the cinchona compounds. The course of rheumatic fever is as speedily checked by large doses of the salicyl compounds.

It is evident that the rheumatic poison, both in its history and in its effects on the system, bears a closer analogy to the poison of malarial fevers than to any other morbific agency.

The poison which gives rise to malarial fever, and that which gives rise to rheumatic fever, are distinct and separate agencies; but the analogies noted in the natural history and course of the ailments which they respectively produce are sufficiently close to indicate the probability of their being allied in nature and in mode of action.

The existence of some points of analogy between intermittent and rheumatic fever did not escape the notice of some of the older observers. Haygarth "thought that there were several analogies between an ague and a rheumatic fever. In both diseases the urine lets fall a similar lateritious sediment. In intermittent as well as rheumatic fever the blood when let is covered with an inflammatory crust.

The pain and fever of rheumatism have certain periodical, though not quite regular, paroxysms and intermissions."

Acute rheumatism is generally regarded as a continued fever; but except its prolonged duration, it possesses none of the characteristics of such a fever. The continued fevers have a regular and continuous course, a typical and characteristic range of temperature, and a definite period of duration; often they terminate by a distinct crisis. Rheumatic fever has none of these characteristics; its course is irregular; it has no definite period of duration, and no typical range of temperature; it never terminates by a distinct crisis, and it is impossible to say how long a case may last if left to pursue its natural course. Seeing a man suffering from one of the continued fevers one can foretell with tolerable certainty the future course and duration of the malady. In rheumatic fever this cannot be done; to-day the temperature may be 104°, and the joints acutely inflamed; a couple of days later the temperature may be 100° and the joints much better; a few days afterward the acute symptoms may have again returned, and the fever be as high as ever; and so it may rise and fall, and rise and fall every few days for several weeks in succession, or the disease may come to a termination at the end of eight or ten days. Irregularity is the prominent feature of both the course and the duration of acute rheumatism. "Irregular pyrexia is joined with irregular perspirations" (Scudamore). It is evident that this fluctuating course is more like that of remittent and intermittent, than that of the continued fevers.

There are reasonable grounds, it will be seen, for regarding rheumatism as malarial in nature, and its poison as a miasm which enters the system from without. The further prosecution of our inquiry necessitates a preliminary investigation into the nature of malarial poisons generally.

The Nature of Malaria.

"I have no hesitation," says Niemeyer, "in saying decidedly that marsh miasm—malaria—must consist of low vegetable organisms." Though when Niemeyer wrote these words our knowledge scarcely warranted so decided a statement, the evidence which has accumulated since then quite justifies it now.

Lanzi and Terrigi, Klebs and Tommasi-Crudeli made a number of observations and researches in the malarial district of the Agro Romano near Rome which led them to believe that the malarial poison is an organism which may be obtained from the soil, and may be cultivated in the bodies of animals.

Laveran, whose researches were carried on in Algiers, found that

the blood of those suffering from malarial fever contained: (1) crescented pigmented bodies; (2) pigmented bodies in the red corpuscles, and (3) pigmented flagellate organisms. These different forms he regarded as different phases in the development of an organism which he believed to be the malarial poison—the cause of the disease. His observations have been amply confirmed by other observers. Osler describes: (1) amœboid bodies in the red corpuscles; (2) pigmented bodies in the red corpuscles; (3) large solid bodies in the interior of vacuoles; (4) free pigmented crescents which may sometimes be seen to develop in the interior of the red corpuscles; (5) rosette forms; (6) scattered small bodies resulting from segmentation of the rosettes; (7) flagellate organisms, round, ovoid, or pear-shaped, with finely granular protoplasm; (8) small, round pigmented bodies one-fourth to one-half the size of the red corpuscles.

The amœboid and pigmented bodies, though met with in both acute and chronic cases, seemed to be chiefly associated with acute manifestations of the disease; while the crescents were noted chiefly in chronic cases and in the later stages of acute cases. Quinine always caused the pigmented bodies to disappear.

Councilman's observations are in accord with those of Osler. The segmented organisms he found chiefly just before and during the cold stage. The crescentic form he found only in malarial cachexia. All forms he found most abundantly in blood taken from the spleen. The effects of quinine on those organisms were carefully noted by him. The administration of this drug in large dose always caused the segmented organisms to disappear; while on the crescentic it had no particular effect. The later researches and observations of Golgi, Manson, and others have fully verified the accuracy of Laveran's observations, and it may be accepted as proved that the organisms which he found in the blood of those suffering from malarial fever are really the poison which gives rise to the disease.

The Mode of Action of Malaria.

Malarial poisons being organisms their morbific action is likely to bear a relation to their reproduction and organic growth. The phenomena of the maladies which they cause are indeed such as can scarcely be explained on any other view. A short residence, even one night, in a malarial district may give rise to a fever of some weeks' duration. If during one night the sufferer inhaled enough poison to cause an attack of fever so prolonged—if the whole of the poison requisite to the production of such an illness existed in and acted on the system at the commencement of the attack, the sufferer

should be speedily killed by a dose competent to produce such an illness. Moreover, if the whole of the poison existed in the system at the commencement of the attack not only would the full effects of the poison be produced at once, but malarial fevers would lose their intermittent and remittent character, and their phenomena be concentrated into a violent attack of continued fever in which recovery would be the exception. It does not seem possible to explain the phenomena of these fevers on the supposition that the whole of the poison necessary to their production exists in the system at the time of onset of the malady. Their varying and intermittent course, their prolonged duration, and their small mortality can be accounted for only on the view that their poisons are reproduced during their course, and that this reproduction takes place in an intermitting manner. And the researches of Laveran, Golgi, etc., have demonstrated that such is the case, the malarial poison being abundantly found in the blood during the pyrexia and not during the apyrexia.

All organisms exercise a definite action on their environment. The environment of these organisms is the blood and the tissues of the body; and what we have to consider is whether or not their action on this environment would suffice to produce the phenomena of malarial fever. The special phenomena which have to be considered are:

1. The occurrence of fever;
2. The occurrence of intermissions in this fever.

The action of minute organisms on their environment essentially consists in the consumption of nitrogen and water. The malarial poison, therefore, consumes the nitrogen and water of the blood and tissues. But as nitrogen and water are the chief elements required for the nutrition of the tissues such an action must have serious effects on the system.

That the reproduction in the system of minute organisms having such an action is competent to cause the essential phenomena of fever I have elsewhere in the case of the continued fevers shown in some detail.

Increased consumption of water causes thirst, dry skin, and scanty urine. Increased consumption of nitrogen means increased metabolism, rise of temperature, increased rapidity of circulation, increased formation and elimination of urea, wasting of the nitrogenous tissues; these are the essential phenomena of fever. The nitrogen and water which ought to go to nourish the tissues are in great part taken up by these minute organisms. Give as much nitrogenous food, as much milk and beef tea as you please, the tissues still waste; give as much water as you please, the thirst, the dry skin, and the scanty elimination of water continue. The nitrogen and water thus supplied

are in great part consumed by the fever poison and do not go to the tissues.

In the muscles such action causes wasting and loss of power; in the heart feebleness; on the skin and mucous surfaces dryness; in the brain the disturbance shows itself by wandering and delirium.

The febrile symptoms of the malarial fevers are to be explained in the same way—their poisons are reproduced in the blood, and consume the nitrogen and water of their environment; and so long as this action goes on the fever continues.

But the question remains, "Why is the fever intermittent?" Malarial poisons grow in and at the expense of the system. They are therefore parasites. It is a rule of almost universal application in the parasite world that each parasite has its own special nidus or habitat in which it is reproduced, and away from which it ceases to manifest life and activity. The parasite of ringworm affects the roots of the hair of the head; that of sycosis the roots of the hair of the mustache and beard; the trichina spiralis makes its nest in muscle rather than in any other tissue; the fluke-worm of sheep makes its home in the liver. In the same way the poison of typhoid fever affects the glands of the small intestine; that of scarlet fever the skin and throat; that of measles the skin and mucous surfaces of the respiratory tract; that of relapsing fever makes a habitat of the blood. Why each of these parasites has its special habitat we do not know; but we know for a fact that it is so, and that each parasite finds in its nidus something which is necessary to its vivification and reproduction, as distinguished from its organic growth, and which it finds nowhere else. It is the existence of the nidus that leads to the localization of each parasitic disease in a particular locality, and so gives to it one of its distinctive features—a special seat; it is its special local lesion which imparts to each of the specific fevers the distinctive features by which it is recognized. Small-pox is known by its eruption, and it is in the matter of its pustules that the poison most abounds. The distinctive feature of typhoid fever is the intestinal lesion; the affected glands are the nidus of the typhoid poison, the special seat of its vivification and reproduction; it is in the discharges which come from them, therefore, that the typhoid poison is most abundant. For the same reason the poison of scarlet fever most abounds in the discharges from the throat and in the peeling cuticle. The only one of the specific fevers which has no local lesion is relapsing fever, its distinctive feature being the relapse; it is also the only one whose poison is found abundantly in the blood. It is a contagious fever, and therefore its poison ranks with the contagia. But though pathologically ranked with the contagious fevers it has many clinical analo-

gies with the malarial. It is in fact a sort of clinical link between the two. It ranks with the specific fevers inasmuch as it is contagious, occurs in an epidemic form, and runs a pretty definite course; it resembles the malarial fevers inasmuch as it has no special local lesion, has for its distinctive feature an intermission, a period of apyrexia between two attacks of fever, and inasmuch as one attack confers no immunity from a second.

If we can explain why it is that relapsing fever has no local lesion, why the fever recurs, and why one attack of the disease confers no immunity from a second, we shall probably find in that explanation a clue to the explanation of similar phenomena in the malarial fevers.

These peculiarities of relapsing fever are all due to the fact that the spirilla which give rise to it find the material necessary to their vivification and reproduction in the blood. The blood is their nidus; and the spirilla are found abundantly in the blood for the same reason that the poison of small-pox is most abundant in the matter of the pustules, the poison of typhoid fever in the discharges from the sloughing intestinal glands, and the poison of scarlet fever in the peeling cuticle and in the discharges from the throat.

The materials requisite to the organic growth of the poisons of the eruptive fevers (nitrogen and water) exist all over the body and are practically unlimited. The special material essential to their vivification and reproduction exists only in the nidus and therefore only in limited quantity. So long as any of it remains the poison continues to be propagated and the febrile symptoms are kept up. When it is exhausted the necessary nidus no longer exists, the propagation of the poison ceases, and the fever comes to an end. That it is the propagation of the poison in the system, and not its mere presence there, that causes the febrile symptoms is proved by the fact that these symptoms come to an end and the patient enters on convalescence while the system still contains much of the poison, as is evidenced by the facts of infection. What brings the fever to an end, then, is not the extinction or elimination of the poison, but the exhaustion of the nidus. Were this nidus to be renewed before the whole of the poison was eliminated, the poison would be reproduced and the febrile symptoms would recur. Such a thing is not likely to happen in the eruptive fevers because the tissues which constitute the nidus are not capable of speedy reproduction; cuticle and intestinal glands are not likely to be formed anew. It is different in relapsing fever. Its nidus is the blood, and the blood is an ever-changing fluid containing nothing which is not likely, when used up, to be sooner or later replaced. As it is the localization of the nidus in a special

locality that gives to each of the eruptive fevers its distinctive and characteristic feature, so it is the localization of its nidus in the blood that gives to relapsing fever its distinctive feature—the relapse. It relapses because the nidus is renewed before there has been time for the whole of the poison to be eliminated from the system.

If such be the explanation of the relapse it is evident that cases may occur in which, either from more rapid elimination of the poison or more tardy renewal of the nidus, the poison is all eliminated before the nidus is renewed; in such circumstances there would be no relapse, the attack being completed in one seizure. That such cases do occur is an established fact in the history of relapsing fever. Of 2,425 cases collected by Murchison 724 had no relapse; of 100 consecutive cases under Murchison's own care 4 were completed by one pyrexial attack; of 400 recorded by Litten 6 had no relapse.

On the other hand it is evident that the process might be repeated more than once, that a third seizure might be caused in the same way as the second, and a fourth in the same way as a third; and so it is found to be. Of 1,500 cases collected by Murchison a second relapse occurred in 109, or in 1 in 14; a third in 9, or in 1 out of 166, and a fourth relapse, *i.e.*, 5 pyrexial attacks, in 1 of the 1,500. The duration of the attacks gets shorter as they go on. In Litten's cases the mean duration of the first attack was 6.6 days; mean duration of the second attack was 4.9 days; mean duration of the third attack was 3.1 days; mean duration of the fourth attack was 3.1 days; while that of the fifth attack was only 2.3 days.

The longer the attack the more poison is produced; so that with each successive seizure there is less poison to be eliminated and a correspondingly greater chance of its elimination being completed before the nidus is renewed. The readiness with which the nidus is renewed probably diminishes also with each successive attack. Thus it very soon happens that the renewal of the nidus is sufficiently delayed to permit of the complete elimination of the poison prior to its renewal, and to the establishment of permanent convalescence. It is in time sure to be reproduced, however, and the blood restored to its former state. One attack of relapsing fever, therefore, confers no immunity from a second.

The same reasoning applies to the case of the malarial fevers—allowance being made for the essential difference between their poisons and that which causes relapsing fever.

They have no local lesion because their poison finds its nidus in the blood. The fever recurs for the same reason that it recurs in relapsing fever—because the nidus is renewed before the poison is eliminated from the system.

The time requisite for the exhaustion of the nidus gives to each of the specific fevers one of their distinctive features—a definite period of duration. It takes on an average about three weeks for the poison of typhoid fever to exhaust its nidus; that of typhus takes two weeks, that of relapsing fever one week. Hence the respective duration of these fevers is twenty-one, fourteen, and seven days; what special ingredient of the blood it is which forms the nidus in relapsing fever we do not know, any more than we know what it is in the intestinal glands that makes them a suitable nidus for the poison of typhoid fever, or what it is in the skin of the hairy scalp which makes it a suitable nidus for the parasite of ringworm. It is some other ingredient which makes the blood a suitable nidus for the poison of intermittent fever.

Recent researches seem to show that this poison, the plasmodium malariæ, finds its nidus in the red blood corpuscles of man. These of course are constantly being renewed; and in this fact we have a possible explanation of the quickly recurring periods of pyrexia and apyrexia which give to malarial fever its intermittent course. On the other hand, the various changes which the plasmodium undergoes in the blood and the various forms which it assumes, render it possible that malarial fevers may owe their intermitting course to these changes and to the peculiarities which are special to the personal history of the poison itself. That is a point which future investigations will settle. What is proved is that the poison of malarial fever is a minute organism which is largely propagated in the blood during the course of the maladies to which it gives rise. That is the point which concerns us at present.

It is in connection with the pathogenesis of rheumatic fever that we have been led to consider the nature and mode of action of malaria. We believe the rheumatic poison to be malarial in nature. If it be so, it is a minute parasitic organism whose morbific action, like that of other malarial poisons, is dependent on its growth and reproduction in the system.

Like other allied poisons it is sure to require, in virtue of its parasitic nature, a special nidus for its reproduction and action. This nidus it finds in the human body. What we have now to do is to explain how a poison having such a nature and such a mode of action produces the phenomena of rheumatic fever.

Rheumatic Fever; or Acute Articular Rheumatism.

The phenomena which present themselves for consideration in this disease are:

1. The occurrence, along with the general febrile disturbance, of a local inflammatory lesion.

2. The almost entire limitation of this lesion (*a*) to such parts of the motor apparatus of the body as are habitually subject to active movement, and (*b*) to the left side of the heart.

3. The tendency of the disease to attack those of a particular age.

4. Its hereditary transmission.

5. The presence in the blood of an excess of fibrin.

6. The presence in the blood of an excess of lactic acid.

7. The occurrence of profuse perspirations.

8. The shifting character of the joint affection.

These we shall consider in the order enumerated.

1. *The Occurrence, along with the General Febrile Disturbance, of a Local Inflammatory Lesion.*—Such association occurs under two different circumstances: (1) The inflammation may precede the fever; or (2) the fever may precede the inflammation. In the former case the fever is the result of the inflammation, and is said to be symptomatic; in the latter its onset precedes the evidence of local inflammation, and it is said to be idiopathic. An instance of the former we have in pleuritis or synovitis following cold or injury; an instance of the latter we have in the bowel lesion of typhoid fever, and in the sore throat of scarlatina.

The first evidence of the existence of acute inflammation of fibrous or serous tissues is pain. The first evidence of febrile disturbance is a feeling of cold and malaise. In purely local inflammations pain is the first symptom. Shivering, malaise, and general febrile disturbance may quickly follow, or may even be contemporaneous with the pain; but they do not precede it. In the local lesions of the specific fevers the case is different. Before their existence can be determined, there is evidence of constitutional disturbance. In the one case the local symptoms precede the constitutional; in the other the constitutional precede the local. Which first show themselves in rheumatic fever? There is some variety in its mode of onset. Usually the patient complains at first only of chilliness and general malaise accompanied by aching of limbs. Soon fever is decided, and the pains are localized in the joints. But one or two days generally elapse before the joints are distinctly inflamed. In milder and subacute attacks, the local joint affection is often the first and only thing complained of; but careful inquiry nearly always elicits the fact that the patient has been out of sorts or has had cold for a day or two before the joint affection declared itself. In whatever way the malady commences, the joint affection is preceded by evidence of constitutional disturbance. But though this is true it is equally the case that the

fever does not reach its height till the articular inflammation is fully established, and that the full development of the fever is contemporaneous with the height of the joint affection. When once the disease is fully established, the local inflammation and the constitutional disturbance go hand in hand—they rise and fall *pari passu*—and there can be no question that the febrile disturbance, though antecedent to, is much increased by, the local inflammation. In this respect the joint inflammation of rheumatic fever resembles the local lesions of the eruptive fevers more than it does common inflammation due to a local cause.

How is the inflammation of the fibrous and serous tissues induced? That it results from the action of the rheumatic poison there can be no doubt. The question is, How does the poison act? It may act in one of two ways: either as a direct irritant of these tissues, causing in them the same kind of excitation that cantharides produces in the bladder, and arsenic in the stomach and rectum; or it may act as an organism and owe its action on the fibrous and serous tissues to its propagation in them.

If its action were that of a direct irritant the course of events in acute rheumatism could scarcely be what it is; for were such its mode of action all the fibrous textures and all the joints should suffer simultaneously and in a like degree; the inflammation would either soon decline or it would become more severe, and would frequently terminate in suppuration; the heart would suffer in every case; and the small joints be as liable to suffer as the large. The gradual onset of the rheumatic inflammation, its shifting character, its uncertain course, its tendency to select certain joints, its occasionally prolonged duration, and its gradual decline, can be best explained on the view that a fresh supply of poison is constantly being brought into play, that the local as well as the general symptoms of rheumatic fever are the result of the propagation of its poison in the system, and that the rheumatic process takes place in the fibrous textures of the motor apparatus because it is in these that the rheumatic poison finds the nidus necessary to its vivification and reproduction. The joint troubles of rheumatic fever are, on this view, the necessary result of the propagation of the rheumatic poison in the structures which are the seat of inflammation, and bear to the general febrile disturbance of that disease the same pathological relation that the local lesions of the eruptive fevers bear to their general symptoms. In the eruptive fevers the distribution of the nidus varies both in situation and extent; it does the same in rheumatic fever. In scarlatina the skin and throat are the nidus; but it is not always equally distributed between the two; when in excess in the skin, there is an abundant erup-

tion and not much sore throat; when in excess in the throat, there is bad sore throat and not much rash. So in measles—the nidus has two seats, the skin, and the mucous surface of the respiratory tract; when concentrated in the skin there is an abundant eruption, and no serious chest complication; when concentrated in the respiratory organs the eruption is scanty, and the chest complications are serious. In rheumatic fever the nidus may exist in many joints or only in two or three; in the former case many joints suffer and the attack is severe; in the latter few suffer and the attack is mild.

In the ordinary forms of malarial fever the poison finds its nidus in the blood; there is, therefore, no local lesion. In rheumatic fever the poison finds its nidus chiefly in the fibrous structure of the large joints. It is in these textures that its vivification and active reproduction take place; it is on them, therefore, that its morbific effects are chiefly manifested. This localization of the nidus in a special structure imparts to rheumatic fever one of the clinical features of the eruptive fevers—general febrile disturbance *plus* a local lesion. As relapsing fever constitutes a sort of clinical link between the eruptive fevers and the malarial, so rheumatic fever is a sort of clinical link between the malarial fevers and the eruptive. The absence of a localized nidus imparts to relapsing fever one of the characteristic features of malarial fever—the tendency to relapse; the presence of such a nidus in rheumatic fever gives it one of the features of the eruptive—a local lesion.

2. *The Local Inflammation is Limited in the Joints Almost Entirely to such Fibrous and Serous Textures as are Associated with Active Movement, and in the Heart to the Left Side.*—The structures which go to form a highly developed joint such as suffers in acute rheumatism are the cartilaginous ends of the bones, a sac of synovial membrane investing these and reflected over the inner surface of the fibrous capsule, the ligaments which bind together and prevent undue movement of the ends of the bones, the tendons of the muscles which move the joints, many of which run in grooves or sheaths having a lubricating surface similar to that which exists in the joint, and the muscles themselves without which the joint structures would be useless. All the structures here enumerated are necessary to the formation and functional completeness of a freely mobile joint. But they do not all equally suffer when that joint is the seat of rheumatic inflammation. It is on the fibrous and serous structures—the muscles, tendons, ligaments, and the lining membranes of the joints and tendinous sheaths—that the action of the rheumatic poison is most manifested.

The symptoms of acute rheumatic inflammation of a joint are pain, swelling, and redness; and the more acute the case the more

marked these symptoms. Pain is the evidence of inflammation of the fibrous textures. Swelling results from inflammation of, and effusion into, the sac of the synovial membrane; redness occurs only in cases in which the inflammation is sufficiently severe to cause hyperæmia of the vessels of the skin; it is, therefore, more common in joints like the knee and wrist in which the inflamed structures are near the surface than in those like the hip and shoulder in which they are more deeply seated. When considering the question of the seat of rheumatism we saw that the muscles participated in the morbid process. It is in them and in the fibrous ligaments and tendons that the morbid process first shows itself; aching tenderness of the limbs and pain in the joints precede swelling; and the question naturally arises whether the inflammation of the synovial membrane may not, instead of being primary, be due to the extension of the inflammatory process to it from the contiguous fibrous textures. There can be no doubt that synovial membrane is very susceptible to inflammation, and that disturbance originating in the fibrous structures of a joint readily extends to it—witness the effusion which follows a strain. We shall by and by see reason to believe that inflammation of the lining and investing membranes of the heart is secondary to prior inflammation of the subjacent fibrous textures of that organ.

3. *The Action of the Rheumatic Poison is Confined Almost Entirely to those of a Particular Age.*—The age of liability to rheumatic fever is from fifteen to fifty. This immunity of the very young and very old can be accounted for only in one of two ways; either the rheumatic poison does not enter their systems, or having entered it does not act. The former is a position which cannot be maintained; for there is no reason why an agency which may gain entrance to the system at twenty or thirty years of age may not equally gain entrance at ten or sixty; the portals of the system are as free and as open at the one age as at the other. The second is a position which may reasonably be maintained, for there is distinct evidence that some poisons may, under certain circumstances, be introduced into the system without producing effect. We know, for instance, that a person who has not been vaccinated and has not had small-pox cannot be exposed to the poison of that disease without almost certainly taking it. But we also know that, having once suffered, he may be constantly exposed, and may even have the poison directly introduced into his system without again suffering from its action. So with each of the eruptive fevers—one attack confers, as a rule, immunity from the future action of its poison. Here we have adequate proof that a poison, and a very potent one too, may gain entrance to the system without producing any effect on it.

We have seen that the rheumatic poison acts on the fibrous and serous tissues of the motor apparatus of the body, and that its action is almost confined to the textures of those joints which enjoy a high degree of functional activity. But these textures are not equally active at all periods of life. In infancy and early life there does not exist the physical strength and stamina necessary for active movement. After the age of fourteen or fifteen matters change; the child has now reached an age at which work and vigorous exercise begin to form part of his daily life; and when adult life is reached hard work and active exercise are of constant occurrence. This implies the constant possibility of vigorous and free movements of the larger joints, and increased force and activity of the heart's action. It necessitates also a state of preparedness for such action. At any time a call may be made for efforts necessitating such movement and action; and the requisite facilitating and restraining forces must be there to meet the emergency. The period of life at which such efforts are made is from fifteen to fifty, or thereabouts. This, therefore, represents the period of highest functional activity of those tissues whose duty it is to facilitate and restrain movement. It also represents their period of greatest liability to the action of the rheumatic poison. The period of liability to the action of the rheumatic poison corresponds exactly to the period of functional activity of the tissues specially involved in that disease. The same thing is noted in connection with some of the eruptive fevers. It is specially marked in the case of typhoid. The intestinal glands whose inflammation constitutes the characteristic feature of that disease exist in infancy in but a rudimentary state. After two or three years they begin to increase in size and functional activity, and go on increasing till adult life is reached. From that time till middle age they are prominent objects in the intestinal wall. They then begin to diminish in size and functional activity and go on diminishing as age advances till in old age they are practically non-existent, and have ceased to exercise any function. The liability to the action of the typhoid poison is directly as the size and functional activity of these glands. In infancy and old age the disease is rare. The period of greatest liability to it is from fifteen to thirty-five. All this is adequately explained on the view that these glands are the nidus of the typhoid poison and are essential to its propagation in the system.

In exactly the same way is to be explained the special tendency of the rheumatic poison to affect people between the ages of fifteen and fifty. This is the period of functional activity of those textures whose inflammation constitutes the special lesion of the disease. They form a suitable nidus for the propagation of the rheumatic

poison only during their period of functional activity; it is during that period, therefore, that the liability to suffer from rheumatic fever is specially manifested.

4. *Hereditary Transmission.*—Many diseases are said to run in families—to be transmitted from father to son. And the facts warrant the statement. A gouty parentage gives a liability to gout. The children of phthisical parents are in turn apt to die of the same disease. Rheumatism is also thus inherited.

But when we say that a man inherits a disease from his father, we do not mean to say that he comes into the world suffering from it, or with its seeds already in him. In the case of gout he may enjoy perfect immunity from it during the greater part of his life and begin to suffer only when forty or fifty years of age. In the case of phthisis perfect health may be enjoyed for twenty years and then the fatal inheritance declare itself. In the case of rheumatism this inheritance seldom declares itself before fifteen, and is generally lost again after fifty.

The son may be born before the father has himself suffered from the malady which he is believed to have transmitted to his offspring. Or the father may even not suffer at all; he may be simply the medium of transmission to his son of a malady from which his forefathers had suffered. Evidently it is not the disease itself, but only the family tendency to it which is transmitted. To transmit an actual disease the father must have its poison in his system when his son is begotten; in which case the child will be born with the malady already developed—as in the case of syphilis. But that is a very different thing from what occurs in the case of rheumatism. What is there transmitted is not the disease but a tendency to it—a greater or less liability to contract it.

This tendency is generally referred to as a constitutional predisposition. But to give it a name is to indicate, not to explain its existence. What is a constitutional predisposition to rheumatism? Wherein does it consist? And what do we mean when we say that a man has inherited rheumatism from his father?

Acute rheumatism consists in inflammation of the fibrous and serous tissues of the motor apparatus. Its poison is a miasmatic organism which is propagated in the system, and finds the nidus requisite to this propagation in those tissues whose inflammation constitutes the special lesion of the disease. For the production of acute rheumatism, therefore, two factors are necessary—first, the poison introduced from without; second, that peculiar condition of the tissues of the motor apparatus which imparts to them their special fitness to act as a nidus for this poison. Which of these factors

is it that is transmitted? Or is it both? One or both it must be, if we recognize transmission at all. It is certainly not both, for their coexistence in the system at birth would give rise to the disease in the infant. As certainly it is not the first, for a miasmatic poison is essentially one which is received into the system from without, and which gives rise to a disease which is not communicable. It can only be the second; it can only be that peculiar condition of the tissues of the motor apparatus which renders them a fitting nidus for the propagation of the rheumatic poison. The difference between a rheumatic and a non-rheumatic subject is that the motor apparatus of the former contains that special ingredient which is requisite to the propagation and action of the rheumatic poison; while that of the latter does not. Between the fibrous tissues of the two men there is no difference that can be detected either by the anatomist or the chemist; but in the one, these tissues afford a nidus for the propagation of the rheumatic poison—in the other they do not. In the one the tissues of the motor apparatus contain something which is wanting in those of the other. It is the presence of this something which constitutes the peculiarity of the rheumatic constitution. It is the tendency to the development of this peculiarity which is transmitted from father to son, and makes each generation susceptible to the action of the rheumatic poison. That such a peculiarity should be inherited consists with all that we know of hereditary transmission. There is no reason why internal peculiarities should not be transmitted as well as external—why a peculiar condition of the brain, of the stomach, of the liver, should not be handed down from father to son as well as a special cast of features, a particular color of hair, a peculiar gait, or a peculiar shape of the limbs. And we know as a fact that certain peculiarities of internal organs are transmitted. Furthermore, there is no reason why peculiarities of individual structures should not descend from generation to generation as well as peculiarities of individual organs; indeed, peculiarity of an entire organ presupposes peculiarity of its individual parts. It consists with all reason that peculiarities of the motor system should be inherited, as well as peculiarities of the nervous, digestive, osseous, and other systems of the body. That some peculiar condition of the motor system is handed down in rheumatism we know. That this condition declares itself by a special susceptibility of the tissues of the motor apparatus to the action of the rheumatic poison we also know. But more than this we cannot say; for in this as in all other cases of hereditary transmission we can only indicate, not explain, the fact. So far as the bearing of this fact on the miasmatic theory of rheumatism is concerned, we can only say that that theory perfectly consists with it.

5. *The Presence in the Blood of an Excess of Fibrin.*—In many forms of inflammation the blood contains an increased quantity of fibrin. In acute rheumatism this excess is specially marked.

Fibrin is a product of tissue waste—an excrementitious rather than a nutrient compound. The evidence of this is that it accumulates during fasting and during many ailments accompanied by increased waste. It exists also in increased quantity in the blood after fatiguing exercise; and Brown-Séquard has shown that the more a muscle is exercised by galvanism the more fibrin does the blood issuing from it contain. There can be no reasonable doubt that fibrin is a product of the retrograde metamorphosis of nitrogenous tissue. We know that inflammation causes increased metamorphosis of the tissue in which it occurs. We know that rheumatism consists in inflammation of the tissues of the motor apparatus. We know that these tissues are the chief source of the fibrin of the blood. We know, therefore, that rheumatic inflammation must be accompanied by increased formation of fibrin. The presence in the blood of an excess of fibrin during the course of acute rheumatism is thus a necessary result of the morbid action which constitutes the characteristic feature of the disease. It results from increased metamorphosis of the nitrogeneous elements of muscle just as excess of lactic acid results from increased metamorphosis of the non-nitrogenous.

6. *The Presence in the Blood of an Excess of Lactic Acid.*—This, one of the characteristic phenomena of acute rheumatism, has already been considered.

It has been shown that lactic acid is a normal product of the retrograde metamorphosis of muscular tissue; that its formation in excess during muscular exercise results from increased wear and tear of the tissues of the motor apparatus; and that its excessive formation in acute rheumatism is due to the same cause, only differently induced. In the one case, the increased metamorphosis results from exaltation of a natural function; in the other, it is a consequence of a pathological process, induced by the action of the rheumatic poison, and leading to excessive formation of lactic acid, in the manner already explained.

The argument may be briefly summed up as follows:

Rheumatism is essentially a disease of the motor-apparatus of the body. Acute rheumatism essentially consists in acute inflammation of the most active parts of that apparatus. The tissues chiefly involved are the muscles and fibrous textures. The rheumatic process must, therefore be accompanied by increased metabolism of these textures. White fibrous tissue contains only nitrogenous material; muscle contains both nitrogenous and non-nitrogenous. Its non-

nitrogenous material is glucose; and it is from this that lactic acid is formed. The difficulty has been to account for the increased metamorphosis of glucose as evidenced by the increased formation of lactic acid. The view which has been advanced as to the nature of the rheumatic process disposes of this difficulty. That poison is reproduced in the muscles and fibrous textures. By seizing on the constituent elements of these, and appropriating them in its growth and reproduction, it causes in these textures the same increased metabolism that naturally results from increased functional activity; in doing this it necessarily causes increased formation of their ordinary metabolic products; one of the metabolic products of muscle is lactic acid. Increased formation of lactic acid is, therefore, one of the results of the rheumatic process; and this increased formation is kept up during the continuance of that process. It results from increased metamorphosis of the non-nitrogenous elements of muscle just as increased formation of fibrin results from increased metamorphosis of the nitrogenous.

7. *The Occurrence of Profuse Perspirations.*—Abnormally free action of the skin is a characteristic of acute rheumatism. As a rule, the more acute the case and the more intense the joint inflammation the more free is this action. The perspiration has an acid reaction, and continues during the whole course of the acute symptoms. By some these sweats have been regarded as exhausting and debilitating, and, therefore, as injurious. By others they have been looked upon as salutary. When two such antagonistic opinions are held we may safely infer that neither expresses the whole truth. In some circumstances profuse perspiration is both evidence of weakness and a cause of increasing debility. In others it is unquestionably salutary, and seems to be the means by which certain disturbances of the system are brought to an end. In rheumatic fever it cannot be said to have either effect. There is no evidence that it causes such debility as results from the night sweats of phthisis; but those who study it in connection with these sweats will naturally draw the inference that it is weakening. There is no evidence that it produces the salutary effects which are noted in connection with the critical perspirations of pneumonia and other acute febrile ailments; but those who study it in connection with these critical sweats will naturally conclude that it is salutary. All cases of phthisis do not have night sweats; they are among the unfavorable symptoms of some cases. All cases of pneumonia do not have critical perspirations; they are among the favorable symptoms of some cases. But all cases of acute rheumatism have acid sweats, and have them not occasionally or at one period only, but continuously through the

whole course of the fully developed disease. There is no evidence that they exercise a favorable influence on the course of the ailment, there is no evidence that they influence it unfavorably. The acid sweats of acute rheumatism are altogether peculiar, altogether different from those noted in connection with exhausting maladies and the crises of acute febrile ailments. They constitute one of the essential symptoms of the disease—one of the invariable results of the action of the rheumatic poison. How are they produced?

The blood in acute rheumatism contains an excess of lactic acid. This it is which gives to the perspiration its acid reaction and odor. As this acid has been regarded by many as the cause of rheumatism its excretion by the skin has naturally been looked upon as a thing to be desired, and this is the foundation for the belief that the profuse perspiration of acute rheumatism is salutary. For so, on this view of the matter, it ought to be. The probability is a hypothetical one, however, which is not supported by fact; for practically we find that the most profuse perspirations afford no relief to the pain. In fact the pain is, as a rule, more severe in cases in which the sweating is most free.

When considering the lactic-acid theory, we saw that one of the most common and constant effects of the internal administration of that acid was increased action of the skin. The dry and branny skin of diabetes becomes under its influence moist and perspiring. If such be the effect of a comparatively small quantity given by the mouth in a disease in which there is great difficulty in getting the skin to act at all, what is likely to be the effect of its formation in large quantity in the system during the course of a malady in which there is no difficulty in getting the skin to act? Clearly, profuse perspiration. That lactic acid is formed in very large quantity in the course of acute rheumatism is evidenced by the quantity eliminated by the skin. Normally it is converted in the system into carbonic acid and water, and in that form is thrown off by the lungs and skin. The elimination of the unchanged acid indicates that there has been formed a larger quantity than can be so converted.

The profuse perspirations of acute rheumatism are due, not to an effort of nature to eliminate the rheumatic poison, but to the stimulant action on the skin of the excess of lactic acid formed during the increased metamorphosis of muscle. These perspirations are to be regarded as neither prejudicial nor beneficial, but as simply one of the essential symptoms of the disease during whose course they occur. They occupy in its symptomatology the same position as increased elimination of urea and bear to the local lesion of rheumatic fever the same relation. The excess of acid is the result of increased meta-

morphosis of the non-nitrogenous, the excess of urea the result of increased metamorphosis of the nitrogenous elements of muscle.

8. *The Shifting Character of the Joint Affection.*—This is one of the most striking peculiarities of a rheumatic attack. In the history of all forms of the disease, acute, subacute, and chronic, it occupies a prominent place; and no theory of rheumatism can be regarded as satisfactory which does not recognize and account for it.

It is impossible to explain it on any theory which recognizes only the existence of a poison equally distributed through the blood, acting like an ordinary medicinal or poisonous agency, and acting, therefore, equally and continuously so long as it exists in adequate quantity; the action of such a poison would be continuous and persistent, not shifting and variable.

The miasmatic theory which regards the rheumatic poison as a parasitic organism requiring for its development and action a second factor or nidus which is localized in fibrous and serous tissues, which exists in varying amount in different parts of these tissues, and which, like the nidus of ordinary malarial fevers, may be exhausted and renewed again, satisfactorily explains this peculiarity of the local lesion of acute rheumatism. Exhaustion of the nidus implies decline of inflammation, its renewal a re-accession to it. Its exhaustion in one joint may coincide in point of time with its renewal in another. In that case the decline of the inflammation in the one will coincide with its onset in the other. In this we have the explanation of the apparent occurrence of metatasis. The inflammation seems to leave one joint and go to another; in reality it is a mere coincidence. The decline of the inflammation in the one has nothing to do with its appearance in the other; by mere accident the second factor is exhausted in the one at the same time that it is renewed in the other. With so many joints liable to disturbance such a coincidence could scarcely fail to occur. Occasionally the metatasis seems to be to the heart; but here too it is a coincidence, for in its tendency to become the seat of rheumatic inflammation the heart is in the same position as a joint.

Treatment.

If the pathology of rheumatism has been unsatisfactory, its treatment has been not less so. There is probably no disease in which so many different modes of treatment have been had recourse to. There is none in which medicinal treatment has until within recent times more completely failed to shorten the duration of the malady. The special mode of treatment in vogue at a given time has generally

depended on the views held regarding the nature and mode of production of the disease. During the last century and the first half of this rheumatism was regarded as a "phlegmasia," as an inflammation dependent, like other inflammatory affections, on exposure to cold, and differing from them only in the nature of the textures involved. The treatment of inflammation was at that time essentially antiphlogistic and consisted in the adoption of various means of depletion. The chief of these was bleeding. Sydenham wrote in 1666, that "the cure of rheumatism is to be sought by blood-letting." His rule was to take ten ounces of blood as soon as he saw the patient, to repeat the operation the following day, to do it again in a day or two, and, for the fourth and generally the last time, three or four days later. But he was not satisfied with the results of this practice; for in 1679, ten years before his death, he says in a letter to Dr. Brady: "I like yourself have lamented that rheumatism cannot be cured without great and repeated losses of blood. This weakens the patient at the time; and if he have been previously weak, makes him more liable to other diseases for some years. . . . Reflecting upon this I judged, it is likely that diet, simple, cool, and nutritious, might do the work of repeated bleedings, and save the discomforts arising therefrom. Hence I gave my patients whey instead of bleeding them." He gives the particulars of a case treated dietetically, in which the patient "recovered his full strength, escaping all such discomforts as ten years before a similar attack, which I treated by bleeding, had entailed upon him."

Cullen, though he regarded blood-letting as "the chief remedy of acute rheumatism," and taught that "large and repeated bleedings during the first few days of the disease seem to be necessary," was careful to add that "to this some bounds are to be set; for very profuse bleedings occasion a slow recovery and, if not absolutely effectual, are ready to produce a chronic rheumatism."

Though the indiscriminate use of the lancet was condemned by many able observers, such as Heberden, Fowler, Latham, and others, bleeding continued, till well on in this century, to be the sheet-anchor in the treatment of acute rheumatism.

"In undertaking the treatment of acute or subacute rheumatism, whether we view the inflammatory state of the aponeurotic membranes as primary and idiopathic, or secondary and symptomatic, it is necessary in the first instance to adopt the antiphlogistic method of treatment, and to carry it on with some degree of energy, and to a considerable extent.

"The different branches of the antiphlogistic regimen requisite in the treatment of rheumatism are blood-letting, general and local, the

occasional employment of cathartics, the occasional employment of emetics, especially tartar emetic, the use of diaphoretics, and the use of revellents.

"*First.* General blood-letting in order to be beneficial ought to be performed early in the disease, and carried to a considerable extent. . . . It should be carried at first to twenty or twenty-five or thirty ounces at once if possible; and within twenty-four hours to as much more.

"*Secondly.* The influence of general blood-letting must be aided by the conjoined operation of various adjuvants. Full vomiting produced by ipecacuanha and antimony is in the majority of cases requisite; and complete evacuation of the bowels by eccoprotics and even cathartics is quite indispensable.

"*Thirdly.* It is of the utmost importance, in attempting the thorough removal of rheumatic pains, to conjoin with blood-letting, or after its use, the administration of full doses of tartrate of antimony.

"*Fourthly.* It is of great moment, if the bowels have been previously well opened, to exhibit, after the first blood-letting, an opiate of forty or fifty minims of the solution of muriate of morphia; or if the bowels have not been freely moved, to effect this indication, and take a second blood-letting, and after this to administer the opiate, which may either be given alone or conjoined with antimony." So wrote Dr. Craigie in 1840. In that year appeared also Bouillaud's "Traité Clinique du Rhumatisme Articulaire," in which the treatment by bleeding *coup sur coup* was advocated with characteristic ability and energy.

To Bouillaud, indeed, belongs the credit of having systematized this mode of treatment. The full extent of his credit in this respect is not generally recognized. Previous to his time the practice of phlebotomy was wanting in method. To take so many ounces of blood, and to repeat the operation in one, two, or more days, was all the recommendation. Bouillaud insisted that there should not be too long an interval between the different bleedings—that the second should be had recourse to before the effects of the first had fully passed off, and the third before the benefit of the second was lost. That is what he meant by his recommendation to bleed *coup sur coup*. It was the frequent repetition of the operation, rather than the quantity of blood taken, which formed the characteristic feature of his mode of treatment. If the pathological views which then prevailed were correct, and if bleeding were the important therapeutic agent which it was believed to be, there can be no doubt that Bouillaud's idea was therapeutically sound. No single dose of any remedy could stop a disease like acute rheumatism. It would have to be

repeated from time to time; and to get its full beneficial effect the second dose would have to be given before the first had quite ceased to act. Bouillaud's merit consists in having applied this sound therapeutic rule to the practice of phlebotomy.

About the middle of this century the practice of phlebotomy and the pathological views on which it was founded were vigorously assailed. Facts tended to show that patients recovered more quickly and satisfactorily when they were not bled than when they were. This was noted in acute rheumatism as in other acute diseases. The rapid accumulation of such facts produced a marked reaction against the old mode of treatment, and within twenty years of the time that Bouillaud's book appeared, the practice of bleeding in acute rheumatism was all but abandoned. Other remedies besides bleeding were used to allay the inflammation.

Purgatives were at one time a good deal used. Those most in vogue were the saline, chiefly the sulphates of magnesia and soda. Calomel was also thus employed, especially by Latham, and with results which gave satisfaction.

Diaphoretics, especially ipecacuanha and antimony in combination with opium, have been at all times much used. Dover's powder has enjoyed a specially high reputation. Referring to it Cullen says: "Notwithstanding what I said in favor of venesection, I must own that I never saw a cure very quickly expedited by venesection alone, in the cure of any violent case of the disease; for the disease is liable to linger, and continue for a long time, and to pass into a chronic state. The Dover's powder gives us an opportunity of more effectually and more safely curing the disease than by bleeding alone."

Opium alone, except as a diaphoretic, was condemned by Cullen; but has had much said in its favor in more recent times by Corrigan, Trousseau, and others.

Cinchona, and its alkaloid quinine, have at different times had their claims to favorable consideration pressed. Morton was the first to use cinchona in acute rheumatism. Cullen gave the great weight of his authority against it. He regarded its employment as "absolutely improper and manifestly hurtful" except in cases in which the acute stage had been subdued by bleeding and other measures, and in which the ailment threatened to become periodic. Haygarth, who first used it on the recommendation of Dr. Fothergill, brought forward much testimony in its favor. George Fordyce used it early and freely. Its alkaloid quinine was at one time freely used, especially in France. A suspicion that it gave rise to cerebral symptoms and dangers prevented many from trying it, notwithstanding the strong recommendations of Briquet, Monneret, and others.

Garrod tried to revive this treatment in a modified form. He gave the quinine along with carbonate of potassium—five grains of the former and thirty grains of the latter, every four hours "until the joint affection and febrile disturbance have completely abated." The benefits which he claims for this plan are its greater efficacy, a diminished tendency to relapse, and a more satisfactory convalescence.

Colchicum has been much used in the treatment of rheumatism; but there is no valid evidence of its exercising any beneficial action. Garrod, who regards its power to subdue gouty inflammation as beyond doubt, says that "it possesses no influence in checking the progress of rheumatic fever." To give relief to the pain of rheumatism it requires to be given in quantity large enough to cause depression of the heart's action; and that is a condition which cannot safely be induced in the course of an ailment which tends specially to affect the heart.

Guaiacum has long enjoyed considerable reputation as a remedy in rheumatism. Originally introduced by Dr. Dawson, it found its chief advocate in Fowler, who regarded it as useful in all stages of the disease. It is nowadays prescribed chiefly in the chronic form. Any good effects which it produces are probably due to its stimulant action on the skin.

Nitrate of potassium was at one time a good deal used as a diuretic and refrigerant in febrile ailments. Brocklesby recommended it in acute rheumatism. He gave as much as two drachms dissolved in some diluent three, four, or five times a day. Given thus, there was got both a diaphoretic and diuretic action. This treatment was revived by Dr. Basham, who not only gave the nitre internally, but also applied it locally to the inflamed joints. The results of this treatment seem to have been as good as those of any other.

Other remedies, aconite, veratrine, digitalis, actæa racemosa, etc., have enjoyed a passing reputation, and had their claims advocated by different observers. But not one of them has stood the tests of time and investigation.

About the time that bleeding went out of fashion, new views began to be entertained regarding the pathology of rheumatism. This was all but inevitable. If bleeding was wrong the pathological view on which that treatment was founded was also likely to be erroneous. If to take blood not only did no good, but even did positive harm, then were there grave reasons for questioning the soundness of what was generally believed regarding the nature of rheumatism. Doubts were started, investigation was stimulated, the symptoms of the malady were subjected to fresh scrutiny, the opinions of the older writers were regarded with a healthy scepticism, and by and by new views

began to be ventilated. The question began to be discussed whether rheumatic inflammation was not altogether peculiar, and due to some special poison circulating in the blood, rather than to the operation of cold. The acid condition of the secretions attracted early and prominent attention, and was regarded as a possible cause of the rheumatism. Prout made the definite suggestion that lactic acid was the rheumatic poison. Ably advocated by Todd, Fuller, and others, this view was soon generally accepted. Altered views of causation led to altered treatment. If lactic acid were the rheumatic poison it was plain that the proper treatment was to promote its elimination and to counteract its effects.

"It is probable that the *materies morbi* in rheumatic fever is lactic acid or some analogous agent. We know that the natural emunctory of this is the skin. Many chemists maintain that it will also escape by the kidneys; and if it ever does so, perhaps this is more likely during rheumatic fever than at any other time.

"Again since vitiated digestion is apt to produce it in undue quantity, and it, therefore, is formed abundantly in the stomach, there is every reason to think a certain proportion of it may be carried off through the alimentary canal. The indications are, then, to promote the action of the skin, the kidneys, and the bowels; to use antacid remedies; and to give large quantities of fluid for the free dilution of the *materies morbi*, and to supply the waste caused by the drainage from diaphoresis and diuresis" (Todd).

The acid theory naturally led to alkaline treatment, and that continued till very recently to be *the* treatment for rheumatism. "If the *materies morbi* be indeed an acid or an acidulous compound—if it be lactic acid, for instance, as there are cogent reasons for believing it to be—then will its neutralization be effected, its irritative property probably diminished, and its elimination promoted, by a free exhibition of alkalies and neutral salts" (Fuller).

The alkaline salts chiefly used have been the bicarbonate and acetate of potassium, given in the dose of fifteen to thirty grains every three or four hours. The evidence adduced by Fuller, Garrod, Basham and others in support of this treatment is sufficient to demonstrate its superiority over any which preceded it. But the sanguine anticipations of its earlier advocates have not been realized; for it has been found in practice that alkalies may be given so as to render the urine alkaline without diminishing the joint pain or allaying the fever.

As time advanced and facts accumulated it became evident that the alkaline treatment did not materially shorten the natural duration of acute rheumatism, or decidedly diminish the tendency to heart

complications—the two advantages which have been specially claimed for it.

We have already seen that the theory on which that treatment is based is untenable, and that lactic acid is not the rheumatic poison, but only one of the results of the rheumatic process.

The theory on which the alkaline treatment was founded being erroneous, we are not surprised to find that treatment fail to produce the good results which its early advocates anticipated.

Impressed with a sense of the failure of this mode of treatment physicians looked about for something better. Owen Rees used lemon juice, and got from it results which were at least as good as those which followed the administration of alkalies. Some gave up all medicinal treatment and simply kept the patient warm in bed, gave him a light simple diet, and administered some *placebo*. Dr. Flint published in 1863 an account of thirteen cases treated on this plan with good results. Two years later an equally good report was given by Dr. Sutton of forty-one cases treated in Guy's Hospital and which got medicinally only mint water.

This expectant plan of treatment was adopted by many with results as satisfactory as those got from more active measures.

"I am quite certain," says Sir Alfred Garrod, "that many cases even of severe rheumatic fever get rapidly well without the administration of drugs; and on simply colored or camphor water the improvement is often so quick and satisfactory that had not the nature of the treatment been known great virtue would surely have been ascribed to it."

This expectant plan of treatment is really that which was recommended and practised by Sydenham in the later part of his career. To treat a patient by mint water, is practically the same as treating him by whey, which Sydenham did two hundred years ago. It is curious to find the physicians of the nineteenth century going back to the same plan of treatment which was recommended by the father of English medicine in the seventeenth.

Sir Russell Reynolds, dissatisfied with the alkaline treatment, tried in acute rheumatism a remedy which had proved serviceable in some forms of spreading inflammation, the tincture of muriate of iron. His results were as good as those got by any other treatment; though his cases are too few to be of statistical value.

Dr. Herbert Davies, reviving an old practice, had recourse to free blistering of the inflamed joints, with very satisfactory results.

Such are the chief remedial measures which had been adopted in the treatment of acute rheumatism up to the year 1876. Antiphlogistic treatment, the alkaline treatment, and expectant treatment,

are the only ones which have met with anything like general approval.

Antiphlogistic treatment was practised, not because of the proved excellence of its results—for two hundred years ago these were regarded as unsatisfactory by Sydenham, and have frequently since then been called in question by others, but because such treatment was the legitimate outcome of the views then held regarding the nature and mode of production of rheumatism.

The alkaline treatment was adopted, not because it has been proved to be specially beneficial, but because such treatment was a therapeutic sequence of the generally accepted acid theory.

The expectant treatment was the practical expression of the opinion which had gradually been gaining ground, that the results of the alkaline treatment were not satisfactory. It succeeded the failure of the alkaline treatment in the nineteenth century, just as in the hands of Sydenham it succeeded the failure of the antiphlogistic treatment in the seventeenth.

A study of the natural history of acute rheumatism led us to the conclusion that the disease is of miasmatic origin, and that the poison which gives rise to it, though specifically distinct, is generically allied to that which cases ague. The ague poison is a minute parasitic organism which finds the nidus necessary to its reproduction in the blood of man. Its morbid action and the symptoms to which it gives rise are a result of this reproduction. The rheumatic poison is a minute parasitic organism which finds its nidus in the muscles and fibrous structures of the joints and of the heart, and the symptoms of acute rheumatism result from its reproduction in them.

The adoption of this view of the causation of rheumatic fever opened up a new field of therapeutic research—and a hopeful one too; for of all diseases malarial fever is that over which drugs exercise most control. Quinine cures ague. That is one of the best established facts in the practice of medicine. Rheumatic fever being similar in nature and mode of production, there might, nay there ought to, be some drug capable of arresting its course as quinine arrests the course of an ague. That is the line of therapeutic research which the miasmatic theory of rheumatism opened up.

A striking fact in the natural history of the malarial fevers is that the trees which provide their cure grow best in countries and localities in which these fevers most prevail; nature seeming to produce the remedy under climatic conditions similar to those which produce the disease.

In rheumatism a low-lying, damp locality and a temperate climate present the conditions most favorable to its occurrence. Looking

about for a plant or tree which most flourishes under such conditions, that which most naturally presented itself was the willow—the various species of salix. Among the Salicaceæ, therefore, a remedy for rheumatism was sought. The bark of most willows contains a bitter principle called salicin. This seemed exactly what was wanted. If the miasmatic theory of rheumatism were correct it seemed not improbable that salicin might exercise on the rheumatic poison the same destructive action that quinine exercises on the poison of ague, and might thus cut short the course of rheumatic fever. It was accordingly tried. The results exceeded all expectation. It was in 1874 that the observations were begun; and early in 1876 the results were given to the profession. They were thus summed up:

"1. We have in salicin a valuable remedy in the treatment of acute rheumatism.

"2. The more acute the case, the more marked the benefit produced.

"3. In acute cases its beneficial action is generally apparent within twenty-four, always within forty-eight, hours of its administration in sufficient dose.

"4. Given thus at the commencement of the attack, it seems sometimes to arrest the course of the malady as effectively as quinine cures an ague, or ipecacuanha a dysentery.

"5. Relief of pain is always one of the earliest effects produced.

"6. In acute cases, relief of pain and a fall of temperature generally occur simultaneously" (Maclagan).

While these observations on salicin were being made, Kolbe, having discovered a method of manufacturing salicylic acid (originally prepared from salicin) from carbolic acid, was bent on finding some use for it. First tried by surgeons as an antiseptic, it was also freely experimented with by physicians in all sorts of diseases, but chiefly in those attended by fever. Its febrifuge properties were soon recognized, and much that was favorable hoped from, and reported of, its action in typhoid fever, diphtheria, erysipelas, pyæmia, etc. But it was soon seen that the disease in which it did most good was acute rheumatism.

Early in 1876, Stricker and Riess published a most favorable account of their experience of its employment in that disease. Their results were quite in accordance with those got from salicin.

The conclusions at which he had arrived are thus formulated by Stricker:

"1. Salicylic acid appears to be a rapid and radical remedy in recent cases of genuine acute rheumatism of the joints.

"2. It is not injurious to the human organism when administered every hour in doses varying from 7½ to 15 grains.

"3. It can be given in these doses for a longer time to young and strong individuals than to the old and feeble.

"4. In the latter it produces toxic symptoms more readily than in the former.

"5. The toxic symptoms vary in degree.

"6. Those most commonly met with are noises in the ears, difficulty of hearing, and diaphoresis; when these occur the administration of the medicine should be discontinued.

"7. If salicylic acid be found to fully answer the expectations entertained regarding it, the internal administration of a certain quantity may be expected to prevent the occurrence of fresh attacks in hitherto unaffected joints, and also secondary inflammation of serous membranes, especially the endocardium.

"8. To prevent relapse, the medicine must be continued in smaller doses for some days after the termination of the main treatment.

"9. Salicylic acid is of doubtful utility in chronic articular rheumatism.

"10. It is not likely to be of use in gonorrhœal or diarrhœal rheumatism, or in the polyarthritis attending septicæmia."

Results so striking could not fail to attract attention. The new drugs were eagerly tried; observations were made on all hands; the journals in England, Germany, France, and America contained numerous reports of cases of acute rheumatism treated by salicin and salicylic acid, and very soon it became a matter of general acknowledgment that these drugs possessed in a remarkable manner the power of shortening the duration and controlling the course of that disease.

In the year following that in which this method of treatment was brought under the notice of the profession, the leading medical journal in England thus referred to the subject: "There are few practitioners who have reported themselves as disappointed in the use of this drug; or, to put it at once strongly and carefully, more disappointed than in the use of quinine for ague. There has not been, in fact, such a consensus of medical opinion on any therapeutic question for many years, as on the power of this drug in one form or other to cure rheumatic fever" (*Lancet*).

The experience acquired during the years that have elapsed since then has amply confirmed the favorable conclusions drawn from the earlier observations, and salicin and salicylic acid are now universally regarded as *the* remedies for acute rheumatism. The evidence, indeed, is now so overwhelming that no one calls in question the efficacy of these drugs, or their power to arrest the course of that disease. To get the full beneficial effects the drug should be given in full and

frequent dose—twenty to thirty grains every hour till the temperature falls and pain is materially diminished. It will generally be found that when the drug is given in this dose the pain and fever are materially allayed in eight or ten hours, and abolished within twenty-four hours from the commencement of treatment. It reads like an exaggeration, but it is a strictly accurate statement to say that treated thus by frequent large doses of salicin or salicylic acid the symptoms of rheumatic fever (pain and fever) are more completely relieved in twelve hours than under the old forms of treatment they used to be in three weeks.

The rapidity with which the cure is effected depends on the dose given; and the necessity for giving the drug in full and frequent dose cannot be too strongly insisted on. Salicin and salicylic acid are rapidly eliminated from the system, and only by giving them in full and frequent dose can their action be kept up. In the early years of this treatment many cases were reported in which these drugs failed to effect a cure. The failures were generally attributable to the inadequacy of the dose given. To give five or ten grains of salicin or salicylic acid every four or six hours is to do injustice both to the patient and to the drug. Large and frequent doses are necessary—thirty grains every hour till pain is relieved and temperature falls; after that the interval between the doses may be widened. But to guard against a recurrence of the symptoms it should continue to be administered for ten or twelve days after all pain has ceased.

It is marvellous how speedily the symptoms decline under this treatment. Relief of pain is the first indication of improvement, and this is generally marked before an ounce of the drug has been consumed, often before half that quantity has been taken. It takes about an ounce of salicin or salicylic acid to completely allay the acute symptoms, and the sooner this is got into the system the better. The cases are few in which that quantity may not be given and pain and fever abolished within twenty-four hours of the commencement of treatment; in many cases this result is got within twelve hours. So rapid is the cure that it is often difficult to keep the patient in bed for more than two or three days. He should never be allowed to get up within a week; for no matter how completely the pain and fever may be abolished, it must be borne in mind that the structures of the joints have been inflamed, and do not at once resume their normal tone on the decline of the inflammation; time must be given for the effects of the inflammation to pass off and the inflamed structures to return to their natural condition.

The following cases illustrate the good effects of the salicyl compounds:

Case I.—A girl, aged 16, never had rheumatism before. Was quite well on April 12th, 1876. On the 13th felt out of sorts, and had a general feeling of cold, with some pain in the limbs. On the 14th the pains increased, and toward evening got very bad. She got up on the 15th and went about as usual, saying nothing to any one about her pains, which were severe in both arms and legs. On the 16th she got up, but was obliged to go back to bed.

April 16th, *vesp.:* Lies in bed unable to move, and every now and then screaming with pain. The back, shoulders, elbows, wrists, knees, and ankles are all the seat of severe pain, but the knees and ankles are most complained of. All these joints are slightly swollen, and so exquisitely tender that the least touch or movement causes her to scream. Has no pain in chest. Skin hot, not perspiring; tongue moist and furred; urine scanty, high colored, and loaded with pink urates. Has a soft blowing murmur with first sound, loudest at apex, but audible over whole heart. Pulse 112, respirations 20, temperature 103.8°. To have fifteen grains of salicin every hour till three powders are taken, and then one every two hours.

17th, *mane:* Wandered at times during the night, but had occasional short snatches of sleep. Pain, especially in ankles and knees, is still severe, but not nearly so bad as yesterday. Can move the right leg a little, and does not complain when the joints are touched. Indeed she allows them to be pretty firmly grasped without complaining; yesterday the least touch made her scream. Tongue furred; skin moist, and perspiration acid. Urine scanty and high colored; bowels confined. Cardiac blow is softer in character, and precedes as well as accompanies the first sound at the apex. Still heard over whole heart, but not so distinctly as yesterday. Pulse 96, respirations 26, temperature 102.8°. Has had eight powders, equal to 120 grains of salicin. To continue to take fifteen grains every two hours.

18th, *mane:* Had a good night, free from pain. To-day feels quite well. Has no pain in any of the joints and can move the limbs without more discomfort than what is caused by a slight feeling of stiffness in the knees. Tongue cleaning; skin natural. Pulse 72, barely perceptible, respirations 20, temperature 99.6°. Has had eighteen powders, equal to 270 grains of salicin.

19th: Slept well; is free from pain, and feels quite well. Wishes to get up. Tongue clean; skin natural; bowels moved; urine abundant, of pale amber color. Pulse 70, feeble, irregular, respirations 20, temperature 98.2°. Has had in all 405 grains of salicin.

The cardiac blow remained, but gave rise to no subjective phenomena. There was no return of the rheumatism. She went on with the salicin for a fortnight.

Rapid as was the cure in this case—the pain having been practically abolished within twenty-four hours, and the temperature brought to the normal within, at the most, sixty hours of the time that treatment commenced—it would probably have been still more rapid had the salicin been given in the full dose in which I now administer it. At the time that Margaret T——'s case occurred (April,

1876) the present certainty regarding the safety as well as the desirability of large doses had not been attained. To such a case occurring now I would give double the dose which Margaret T—— got; and probably with a more rapid result, as in the following case, which bore a close resemblance to hers:

CASE II.—A girl, aged 17; had always enjoyed good health. With the exception of measles and scarlatina in childhood never had any ailment.

On May 26th, 1878, she felt out of sorts and had such aching in the limbs that she did not leave the house. On the following day she was worse and toward night got very bad.

May 28th: Lies in bed, unable to move, the least effort to do so causing intense pain, and making her scream. Has anxious, pained expression. The knees and wrists are most painful, but the ankles, right shoulder, and neck are also complained of. The affected joints are a little swollen, and exquisitely tender; except over the wrists, there is no redness of the surface. Tongue moist and furred. Skin hot and perspiring; bowels moved by medicine; urine scanty, and loaded with urates. Heart's sound normal. Pulse 112, respirations 22, temperature 103°. To have thirty grains of salicin every hour till decidedly relieved.

She began to take the medicine as 6 P.M., was then in great pain. She felt easier after the third powder, and after the fifth (taken at 10 P.M.) was so decidedly relieved that she fell asleep. Her mother, who remained beside her all night, stated that she would probably have slept on, but that she woke her up to give the salicin at 11 o'clock, and at midnight. After that, she had a powder only every second hour.

29th: Has a pleased, smiling expression. Is quite free from pain, except when the joints are pressed; allows one to grasp them, and can move them without more than a feeling of stiffness. Thinks she would have slept all night if her mother had not wakened her to give the medicine. Perspired a good deal during the night. Skin is now covered with acid perspiration; saliva acid; tongue cleaner; pulse 88, respirations 20, temperature 99.8°. Heart's sounds normal. Up to this time (9:30 A.M.) has taken eleven powders, equal to 330 grains of salicin. To have thirty grains every two hours.

7 P.M.: Has had no pain, and says she would like to get up. Complains only of a slight degree of deafness. This her mother noticed before the patient did. Has perspired a good deal; reaction acid. The joints feel stiff when she tries to move them, but can be firmly pressed without pain. Pulse 76, respirations 20, temperature 98°. Heart's sounds normal. Has had in all exactly one ounce of salicin, 16 thirty-grain doses.

She continued to take the salicin in gradually diminishing dose for four days, during which she was kept in bed. At the end of that time she was allowed to get up, and the salicin was given in twenty-grain doses four times a day for a week longer. She made a perfect recovery and had no return of pain.

In this case the acute pain was abolished within six, and all joint tenderness within twenty-four, hours of the time that treatment commenced. Within that time, too, the temperature had fallen from 103° to the normal standard, a fall of five degrees. The case was a very acute one.

Case III.—A man, æt. 30, robust and well built, had rheumatic fever for the first time four years ago. Was then two months in bed, and three off work.

December 31st, 1878: Two days ago was seized with pain in the right knee. Yesterday the right was a little better, but the left became very painful. To-day the right shoulder and left ankle are also affected. Had little or no sleep last night from severity of pain. Tongue furred; bowels moved by medicine; urine high colored, and depositing pink urates; skin moist; perspiration acid; pulse 100, respirations 22, temperature 101°. Heart normal. To have thirty grains of salicin every hour for six hours; then every two.

January 1st, 1879: Felt better after four powders, and by night was so relieved that he slept well, waking up only twice—on each occasion taking a powder. Has taken altogether ten of them, equal to 300 grains of salicin. Is quite free from pain. Felt so well this morning that he got up and dressed, and at time of visit was walking about the house. Was ordered to go to bed. In bed is quite free from pain; but when walking about the left knee and ankle hurt. Skin covered with acid perspiration; urine less scanty, of amber color, with slight deposit of urates. Heart normal. Just after getting into bed the pulse was 88, respirations 20, temperature 98.8°. A powder every two hours.

He perspired very freely during the day and in the evening felt so well that he got up again for a couple of hours.

2d: Slept well at night. Took no powder between ten last night and seven this morning. Has had in all eighteen powders, equal to 540 grains. Perspiring freely—secretion acid; has no pains; swelling and tenderness quite gone; pulse 72, respirations 18, temperature 98.3°. He was ordered to take the salicin three times a day for ten days. He remained well and resumed work on the 8th of January. In this case the attack was abolished within twenty-four hours.

Case IV.—A man, æt. 34, has twice had rheumatic fever, once at 18, and again at 24. On each occasion was laid up for six weeks. Present illness began three days ago with malaise and aching in limbs. Pains have steadily got worse and have become localized in the joints.

November 4th, 1878: Skin hot; expression anxious; tongue furred; urine high colored and scanty; pulse 116, respiration 24, temperature 102.5°; ankles, knees, right shoulder, and fingers of the right hand are swollen and painful. The heart's sounds are normal. To take thirty grains of salicylate of soda every hour till pain is relieved; after that, every two hours.

5th: Is much better. Felt easier after the third dose of the medicine. Had a good night, but perspired a great deal. Is now covered with acid perspiration; saliva is also acid. The swelling is all but

gone from the joints, and there is no pain except when they are moved or pressed. Heart normal; pulse 92, respirations 20, temperature 99.6°. Took the medicine every hour for four hours. He was then easier, and took it every two hours. Has had in all nine doses, equal to 270 grains. Says he feels a little squeamish after it. To take a dose every three hours.

6th: Feels quite well, only weak. There is no swelling, and no pain even on pressure over the joints. Acid perspirations continue. Pulse 70, respirations 18, temperature 98°. Heart normal.

He remained well; but took the salicylate three times a day for ten days.

Case V.—A man, æt. 22; never had rheumatism before.

December 12th, 1877: Present attack commenced four days ago with sore throat and general aching. Now the pain is localized in the left knee, both ankles, and right shoulder. Except the shoulder, the affected joints are slightly swollen, and all are distinctly tender, though the pain is not very acute when he is at rest. Any movement aggravates it much. The skin is covered with acid perspiration; tongue furred; urine high colored and loaded with fawn-colored urates; bowels moved by medicine; heart sounds normal. Pulse 104, respirations 28, temperature 100.8°.

To have twenty grains of salicylate of soda every hour till pain is decidedly relieved; then every two hours.

13th: Is much better. Was decidedly relieved after five or six doses of the medicine, but went on with the hourly dose for eight hours. After that he fell asleep, and woke up only now and then during the night. Has had up to this time (11 A.M.) thirteen doses, equal to 260 grains of the salicylate. The joints are stiff and slightly swollen, but the pain is gone. Perspires freely; secretion acid. Pulse 84, respirations 20, temperature 98.8°.

14th: Pulse 68, respirations 18, temperature 98.2°. Heart normal. Took the salicylate four times a day for four days, and thrice a day for a week more. Remained well.

These cases suffice to illustrate the controlling power exercised by the salicyl compounds over the rheumatic process.

In young subjects, and in those who have not suffered from repeated rheumatic attacks, such is generally the course of events, if the remedy is given in sufficient quantity, and for a sufficient time. But it is of importance that these two conditions should be observed; for if given in insufficient quantity the desired result is got slowly or not at all, and if omitted too soon the symptoms are apt to recur.

It has been said that acute rheumatism is more apt to relapse when treated by the salicyl compounds than when treated by alkalies. It is not so, if the salicyl treatment is properly applied. When treated by alkalies the treatment is continued for several weeks and is omitted when the temperature is normal and pain has ceased. But this result is not due to the treatment. The disease has run its natural course and worn itself out. For that reason there is no tendency

to relapse. But when treated by the salicyl compounds the course of the disease is arrested and the temperature falls to the normal standard in a few hours. If treatment be omitted as soon as this result is attained the symptoms are likely to recur, for though the rheumatic process is arrested the rheumatic poison is not all destroyed; what remains is reproduced and the joint pains and fever reappear. It is not a true relapse, but a recrudescence of the symptoms consequent on the too early omission of the drug, a result which may readily be guarded against by continuing the treatment for a time after acute symptoms have disappeared.

To effect the complete destruction of the poison and ward off the chance of recrudescence or relapse the drug (salicin or salicylic acid) should be continued for a week or ten days after all rheumatic symptoms have disappeared. When this is done the complete destruction of the poison is insured, and the disease does not relapse.

To get the full benefit of the salicyl treatment two things are essential:

1. The drug must be given in full and frequent doses till the temperature is normal and the pain gone;

2. It must be continued in smaller doses for ten days after all acute symptoms have ceased.

The two following are cases in which the early omission of the treatment was followed by a return of the rheumatic symptoms.

Case VI.—A woman, aged 25, seen March 2d, 1878, had rheumatic fever five years ago, was then laid up for two months. Present attack began five days ago with aching in the limbs.

March 2d: Face flushed and anxious, skin covered with acid perspiration, tongue furred, urine loaded with urates; right knee, both ankles, and wrists swollen and very painful; pulse 104, temperature 102.4°. Heart normal. To have light diet, and thirty grains of salicin every hour till pain is relieved; then thirty grains every two hours.

3d: Took a powder every hour for five hours; after that felt easier, and took one every two hours while awake; has had in all thirteen powders, equal to 390 grains. Is now free from pain; the joints are stiff and slightly swollen, but not tender; pulse 80, temperature 99.8°; skin covered with acid perspiration; bowels moved; heart sounds normal. To have a powder every two hours till a dozen are taken; and then one every four hours for a week, and to remain in bed for that time. The patient felt so well that she neglected these precautions; got up on the 5th, and took only an occasional powder after that time. On the 8th the joint pains returned.

9th: Knees, ankles, and wrists inflamed; acid sweats; pulse 100, temperature 101.9°. To have thirty grains of salicin every hour for six hours; and then every two hours.

10th: Is free from pain; pulse 76, temperature 98.5°. Has had 360 grains of salicin. To continue it every three hours for four days,

and after that, four times a day for ten days. This time she did as directed, and remained well.

In this case there can be no doubt that the relapse was due to the too early omission of the salicin.

What happened was as follows:

The salicin was taken, during the first attack, long enough and in sufficient quantity to allay the symptoms and nearly but not quite destroy the whole of the rheumatic poison. What remained was reproduced, and gave rise to a renewal of the rheumatic symptoms. On the second seizure the drug was taken for a sufficient length of time, and in sufficient quantity to destroy the whole of the poison. Convalescence was therefore permanent.

Case VII.—A man, æt. 44, had rheumatic fever when he was 28 years of age, again when he was 30, a third time when he was 33, and a fourth time when he was 37. On the first occasion he was confined to the house for three months, and was unfit for work for other six, nine in all. The second attack was equally long. During the third and fourth attacks he was in bed for six weeks, and off work for three months. Was always treated by potassium.

A fortnight ago he began to suffer from twinges of pain in the back, neck, and right leg. Two days ago got much worse, and was obliged to take to bed. For two nights the pains have been so severe that he has had no sleep.

December 1st, 1878: Has an anxious expression; tongue furred, bowels confined, skin perspiring; perspiration and saliva acid; pulse 116, respirations 30, temperature 102.1°; has great pain in the left heel, all along the right leg, and in the knee and hip joints of the same side. The neck and the right wrist and hand are also painful and tender to touch. The affected parts are tender, but not red or distinctly swollen. The breathing seems a little oppressed. The heart's sounds are free from *bruit*, but are muffled in character; and there is a slight click with the systole. To have an aperient, and thirty grains of salicin every hour.

2d, *mane:* Took a powder every hour till 4 A.M. At that hour he fell asleep, and slept on till eight. Has had up to this time sixteen powders, equal to one ounce of salicin. States that he has no pain, only stiffness of the joints and limbs; can bear firm pressure everywhere. Indeed, he felt so well that he got up and at the time of the visit was sitting in front of the fire, free from pain but stiff and weak. Skin acting freely, perspiration and saliva acid; pulse 100, respirations 28, temperature 98.4°. States that he can scarcely believe it possible that he is so well. To remain in bed and take thirty grains of salicin every two hours.

Vesp.: Has been quite free from pain; so much so that he neglected his medicine, and went from his room into a cold water-closet. Has no pain; but the pulse is 108, the respirations 30, and the temperature 101°. There is a slight click with the first sound of the heart,

but the muffled character of the sounds has disappeared. To remain in bed, and take a powder every hour.

3d: Had a good night; slept from ten till three without waking; felt quite well then; got up and went to another room to see what o'clock it was; felt weakened and chilled by doing so; slept again from four till seven. Has no pain, but feels weak; perspiration abundant and acid; pulse 92, respirations 28, temperature 98.1°. To have salicin (30 grains) every two hours.

4th: Passed a very good night, awake only once for a short time; feels quite well; heart's sounds normal; acid perspiration continues; pulse 76, respirations 20, temperature 98.2°.

At this time I ceased to visit him, but gave strict injunctions that the salicin was to be taken in thirty-grain doses every four hours for a week. Five days afterward I was sent for to see him again.

Stated that he felt so well that he did not take the medicine regularly, as instructed, but took only half a powder occasionally.

Practically the salicin was omitted on the 5th, and on the 7th he put on his clothes and went about the house. The weather at this time was bitterly cold.

On the 8th the pains began to trouble him again.

9th: Has pain in both ankles and right wrist, all of which are swollen and very tender, but not red. Skin hot, not perspiring; pulse 100, temperature 100.3°. Heart's sounds normal. To have thirty grains of salicin every hour.

10th: After taking five powders (150 grains) he fell asleep, and passed a good night, waking only once. Pain is gone, only stiffness and slight tenderness on pressure remaining; heart normal; pulse 100, temperature 102.7°. Continue salicin every hour. Has had 210 grains in all.

11th: Has scarcely any pain, but feels wretched and out of sorts; the joints are not swollen, but are more or less tender on pressure; perspiration acid, not very abundant; pulse 100, temperature 101.5°. Heart normal. Has had 540 grains of salicin. To have thirty grains of salicin and fifteen of bicarbonate of potassium every two hours.

12th: Is much the same, no special pain, but the tenderness on pressure remains; perspiration slight but distinctly acid; pulse 100, temperature 101.3°. Continue powders. Has had 750 grains of salicin.

13th: Feels much better; pain and tenderness gone; pulse 90, temperature 98°. Has taken 930 grains of salicin.

14th: Feels quite well, only weak; pulse 76, temperature 98°. Has a good appetite.

He was more careful on this occasion, remained in bed for a week, took salicin for a fortnight, and made a good recovery without any drawback.

In this case the pain was decidedly relieved within six, and was gone within twenty, hours of the time that he came under notice. The temperature, too, had fallen to the normal standard.

It will be noted that during the first attack neglect of the salicin, on December 2d, led to a rise of the temperature from 98.4° in the

morning to 101° in the evening. The resumption of the remedy in hourly doses led to a speedy fall of the temperature to the normal. The second attack was clearly attributable to the early omission of the salicin.

Reference has already been made to a morbid condition to which the term rheumatism is usually applied, but which is more properly a sequence of rheumatism than a distinct form of the disease. The condition referred to essentially consists in chronic thickening and irritability of fibrous textures which have been the seat of frequent attacks of rheumatic inflammation. The usual history of such cases is that each attack has been less perfectly recovered from, leaving behind it a legacy of increased disability. Their history indeed shows, what a knowledge of pathology would indicate, that the textures which have been the seat of inflammation do not recover their natural tone as soon as the inflammation ceases. There remains for a time, which varies with the length and severity of the seizure, some thickening of the fibrous textures of the affected joints, causing the stiffness which is felt after the acute symptoms have disappeared. If the attacks are frequent and obstinate this morbid change in the fibrous textures is less and less perfectly recovered from, by each succeeding seizure a little more damage is done, and ultimately there is induced a condition of chronic thickening of these textures, which is permanent.

That such a change should take place as a result of frequent and long-continued rheumatic attacks consists with what we know of the mode of production of similar pathological changes in other organs.

Clinical experience teaches that when an organ has been the seat of repeated attacks of inflammation, the local symptoms to which such inflammation gives rise are apt to recur in a minor degree from the operation of causes which would not have sufficed to induce the original attack. What more common than for chronic bronchitis to be developed as a sequence of one or more acute attacks; and for the course of the chronic malady to be interrupted by subacute seizures brought on by causes which would not have sufficed to induce the original malady? A similar instance we have in the readiness with which dysenteric symptoms may be developed in those who have once suffered from the acute form of the disease. Exposure to cold, overfatigue, mental disturbance—causes which never could have originated the disease—will often bring back some of the local symptoms of the original attack in a milder but still quite characteristic form. So it is with fibrous textures which have been weakened and altered by repeated rheumatic attacks. They are rendered irritable and weak by the changes which have taken place in them, and are apt to be dis-

turbed by agencies which have no such effect on healthy fibrous textures. Irritation of fibrous textures, no matter how induced, causes pain in the affected part. Hence such disturbance as arises in these altered textures from exposure to cold and damp gives rise to the same symptoms as would result from the action of the rheumatic poison. Originating in true rheumatic attacks, occurring in those who have given decided evidence of being of rheumatic constitution, and characterized by symptoms which are associated with true rheumatism, it is not unnatural that the symptoms should be regarded as due to the action of the rheumatic poison. But such a view is pathologically inaccurate and pregnant with therapeutic errors. The condition which has to be dealt with is one which, though originally induced by repeated rheumatic attacks, exists, after it has been developed, independently of the cause which gave rise to it. Pain, swelling, slight rise of temperature, even increased formation of lactic acid, may thus result from inflammation of these altered fibrous textures induced by cold, just as like symptoms would result from similar disturbance set agoing by the rheumatic poison. We may thus have all the symptoms of subacute rheumatism without any action of the rheumatic poison. Over such an attack the salicyl compounds can exercise no control.

If the subacute exacerbation be due to the action of the rheumatic poison—to a fresh rheumatic attack—the salicyl treatment will do good for a time, but will fail to cure because the irritable textures will take some time to regain their normal condition after the rheumatic poison has ceased to act, and because the lactic acid, formed as a result of their inflammation, tends to keep up disturbance in them. Such a case treated by salicin or salicylic acid would be, and with justice, instanced as one in which these drugs gave only partial and temporary relief.

It is in these cases in which the fibrous textures have been the seat of prior attacks of rheumatic inflammation that the alkaline treatment often does much good. The change resulting from the former attacks renders these textures more irritable and more liable to disturbance from the presence of lactic acid. As a consequence of this, the local symptoms are apt to persist for a time after the action of the rheumatic poison has ceased. They are kept up by the lactic acid, and anything which hastens the elimination of this from the system tends to shorten the duration of the attack. Hence in such cases the alkaline treatment should be combined with the salicyl. The latter puts a stop to the rheumatic process; the former aids in the elimination from the system of the lactic acid formed during that process.

As compared with the frequency of the occurrence of the acute and subacute forms of rheumatism in which it originates, this chronic thickening of the fibrous textures is not common, at least in its fully developed form. For this there are two reasons: first, it is only in a minority of cases that the rheumatic constitution is so marked as to lead to attacks sufficiently frequent and long-continued for its production; and second, in a large number of those who possess this markedly rheumatic constitution, the heart suffers as well as the joints, and death ensues from the cardiac trouble, before there has been time for the development of permanent thickening of the fibrous textures.

Nowadays, treatment is so successful in shortening the duration of acute and subacute rheumatism that it may reasonably be hoped that this condition will year by year become less common.

This thickening of the fibrous textures is a condition over which drugs exercise little or no control. As one can never be sure that the pain at a given time may not be due to the action of the rheumatic poison, the salicyl compounds should always be given for a time, not with the idea of removing the chronic thickening, but with the object of relieving any purely rheumatic symptoms. For those who can afford it the most useful treatment is such as is to be got at Bath, Buxton, Droitwich, Strathpeffer, and other baths in Great Britain; at Aix-les-Bains, Dax, in France; at Aix-la-Chapelle, Wildbad, Gastein, Teplitz, Wiesbaden, Franzensbad, and other baths in Germany.

Chronic rheumatism is the ailment for which this chronic thickening of the fibrous textures is most apt to be mistaken. Occurring as it does in those who have suffered from repeated attacks of acute or subacute rheumatism, and presenting many of the symptoms of rheumatism, it could scarcely fail to be mistaken for the chronic form. It is of great importance that the two conditions should not be confounded, for their prognosis and treatment are essentially different. Wherein chronic thickening of the fibrous textures consists, its name implies. Its pathology we have just considered. Chronic rheumatism, properly so-called, is a very different condition. It is due to the presence and direct action of the rheumatic poison, and is not necessarily, or even usually, accompanied by any perceptible change in the textures involved. It consists simply in rheumatic disturbance of the affected tissue. It differs from the acute and subacute forms not in nature but in degree, and sometimes in the special textures involved. It is a true rheumatic attack in which the morbid process and local disturbance are not sufficiently marked to raise the temperature or to lay the patient up. The textures involved are the same as those which suffer in the acute and subacute forms, with this

difference, that the fibrous aponeuroses and muscles are more apt to be affected.

Chronic articular rheumatism usually affects the same joints as suffer in the acute and subacute forms. Seldom more than one or two joints are affected at the same time, and in none of them is the pain bad enough to lay the patient up. It may shift from joint to joint and last, off and on, for months or even for years, the patient during the whole time being never really ill and yet never quite well for more than a few weeks at a time.

The following two cases serve to illustrate this form of the disease.

Case VIII.—A woman, æt. 34, the mother of seven children; had rheumatic fever when she was 15. Was in bed for three months at that time. At 27 had a second but much milder attack which lasted only for eight or ten days. States that she had been subject to joint pains almost ever since her first attack. Is frequently quite well and free from pain, but for last six months has had it very constantly, but never bad enough to prevent her going about.

May 12, 1877: Has been ailing all the winter. For last six weeks has not been out of the house, as going out always made her worse. Has now pain and stiffness of knees, ankles, and wrists; the last are a little fuller than natural. Heart normal; pulse 70, temperature 98.5°. To have thirty grains of salicin every three hours.

14th: Feels better than she has done for months. Pain nearly gone. Has taken thirteen powders, equal to 390 grains of salicin.

16th: With the exception of a little stiffness of the joints feels quite well. Is free from pain.

A year and a half afterward she consulted me about one of her children. Told me that the salicin did her so much good that she had taken it, off and on, almost ever since. Has never enjoyed such good health, or been so free from pain as during the last year.

Case IX.—A man, æt. 35. Had an attack of rheumatic fever when 18 years of age. Was laid up for two months. Has suffered from occasional pains in the joints almost ever since. Thinks he has never been more than three months together quite free from pain. Its usual seats are the knees, ankles, and wrists. Generally only one joint is affected at a time. For the last few months the pain has been more troublesome, especially in the right knee.

December 8th, 1878: Has pain and stiffness of the right knee and ankle. Neither joint is swollen, but both are tender on firm pressure. Heart sounds normal; pulse 74, temperature 98.6°. To have thirty grains of salicin every two hours.

9th: Feels decidedly better.

11th: Is free from pain and more comfortable than he has been for many months. Has had in all 360 grains of salicin.

He continued it three times a day, in twenty-grain doses, for several weeks; and by my advice took it for some months twice a day.

In December, 1879, he wrote to me as follows:

"It is just a year since you prescribed the salicin for me. I thought it might interest you to know that I have continued to take

it ever since, off and on. The dose I take is twenty grains once or twice a day. I have never passed more than a week without it. I was never better in my life than I have been during the past year, and never so free from pain."

The heart is less apt to suffer in the chronic than in the acute and subacute forms; but it does sometimes become involved. The cardiac trouble partakes of the general slowness of the ailment, and is seldom detected till the patient begins to suffer from some of the subjective phenomena of heart disease.

Muscular Rheumatism.

Instead of affecting the joints rheumatism sometimes attacks the muscles and their aponeurotic covering. Its chief seats are the large muscles of the thighs, back, shoulders, and arms. It causes pain in the affected part, increased by movement and pressure. The pain is not so apt to shift about as in the articular form of the malady. The ailment for which it is most apt to be mistaken is neuritis. In muscular and aponeurotic rheumatism the pain is diffused over the affected muscles and aponeuroses, and one part is not much more tender to pressure than another. In neuritis the tenderness on pressure is less diffused and is felt more at points here and there along the course of the nerves. The pain is apt to be seated in a particular set of nerves; the brachial plexus being a common seat of it. In chronic muscular rheumatism the pain is increased on movement; in chronic neuritis it is apt to be worse at night when quiet in bed.

The following cases illustrate this form of rheumatism.

Case X.—A woman, æt. 25; had for several months suffered, off and on, from pains in the shoulders, loins, and right thigh, which had got worse during the last few weeks. Pain is increased by motion. Never had rheumatic fever or any affection of the joints. She has no other local ailment, but feels weak and out of health. This she attributes to pain and want of sleep. Pulse and temperature normal. To have twenty grains of salicin every two hours till the pain is relieved; and then three times a day for a fortnight.

Three weeks later she again consulted me. Stated that the powders quite cured her in three days, and that she then omitted them. A week after she omitted the salicin, the pains returned in the old localities. It was again given in twenty-grain doses every two hours for three days; after which time she was ordered to take a powder three times a day for three weeks. This she did, and with the result that the pain disappeared, her general health improved, and she remained well.

Case XI.—A woman, æt. 28; never had articular rheumatism; has suffered for six weeks from pain in both thighs, hips, and lumbar region. Affected parts are somewhat tender to pressure made with

the point of the finger, but not to similar pressure made with the palm of the hand. The tenderness is most marked over the upper and outer parts of the thighs. Has been rubbing on various anodyne and stimulant applications without relief. Pulse and temperature normal. To have twenty grains of salicin every two hours. On the following day she was decidedly relieved; and on the next, after having taken in all 360 grains, was all but free from pain. She took twenty grains of salicin three times a day for a fortnight, and remained well.

As will be seen from these cases, the treatment of this form of rheumatism is not different from that of the articular form of the disease.

The Mode of Action of the Salicyl Compounds in Rheumatism.

Holding, as we do, that the poisons of rheumatism and of ague, though specifically distinct, are similar in nature and in mode of action, and finding that the morbid process to which each gives rise may be arrested by large doses of somewhat similar remedies, we cannot but regard it as at least probable that the mode of action of the remedy is the same in both—that the salicyl compounds cure rheumatic fever in the same way that the cinchona compounds cure intermittent.

That the cinchona alkaloids arrest the course of intermittent fever is an established fact in practical therapeutics. How they do so has never been explained. "Ague is the disease of all others in which the power of medicine, both as regards prophylaxis and treatment, is most marked. We know that if a man pass through certain districts, and more especially if he sleep in them, he is likely to be attacked with a fit of shivering which, after lasting some time, will be succeeded by a burning fever, and then by profuse sweating, after which he will feel comparatively well until the next day, when another shivering fit will come on at the same hour, and run the same course as the first. We know that by warning the man against the dangerous locality, or by making him adopt certain precautions, take cinchona alkaloids if he cannot avoid the place, we may be able to prevent the disease; by administering one large dose of quinine before a paroxysm we may stop its approach, and by continuing the remedy we may prevent its recurrence altogether. But we have no notion of the manner in which quinine counteracts the malarial effects" (Lauder Brunton).

There are two ways in which the curative effects of quinine in ague may be produced; either the quinine may so act on the system as to render it unsusceptible to the action of the ague poison, or it

may so act on that poison as to deprive it of its power of affecting the system. In other words, the action of quinine is either on the system or on the poison. Let us inquire which it is. First, as to its action on the system.

Quinine in large dose (10 to 30 grains) possesses in a remarkable manner the power of lowering the temperature of the body, when unduly elevated; how it exercises this power is not known. It has been supposed to be due to a special action of the quinine on the nervous centres; and if we recognize the existence of a special thermic centre, regulating the production and distribution of heat, as the vasomotor centre regulates the distribution of the blood, this explanation is a very feasible one. Binz thinks this effect of quinine is to be explained by its lessening the ozonizing power of the blood, and so checking oxidation. All that we really know, and all that concerns us at present, is that quinine in large dose lowers febrile temperature. What we have to consider is whether or not its curative effect in intermittent fever is due to this property, or to some other and special remedial action.

In virtue of its febrifuge properties, quinine has been administered in all febrile ailments. It was at one time claimed for it that it possessed the power of cutting short typhus. More recently it has been claimed for it, as for other febrifuge remedies (the cold bath and salicylic acid) that it exercises a distinctly curative action in typhoid fever, and shortens the duration of that malady. But this conclusion is not supported by the evidence. There is no proof that quinine either shortens the duration or lessens the danger of either typhus or typhoid fever, or that it exercises a distinctly curative and curtailing effect in any other form of fever than intermittent and remittent. The point is one which could be readily proved, and would long ago have been proved, had the facts been as some have stated them to be.

I have frequently given quinine in large dose in all febrile ailments. My experience entirely coincides with that of Murchison, who says, with reference to both typhus and typhoid fevers, that he had seen no evidence that, at whatever stage it was given, it shortened the course of the disease or diminished its danger.

In intermittent fever the case is very different. Here the quinine actually cures. It puts a stop to the whole morbid process, and all that constitutes the disease; and it does this so constantly, so speedily, and so certainly, and its beneficial effects are so lasting, that one cannot fail to see that they are altogether peculiar and altogether different from those got from its administration in other febrile ailments.

That the action of quinine in arresting the course of intermittent

fever is not to be explained solely by its febrifuge properties, is further shown by its power of preventing such fever. Given during the intermission it prevents the fever from coming on. It exercises a distinctly prophylactic action. Taken regularly by those living in malarial districts, it prevents them from suffering from the action of the poison of intermittent fever. It exercises no such action in any other febrile ailment.

Besides its febrifuge property quinine possesses no other special action on the body by which its curative effect in ague can be explained. This property does not account for its remarkable power of arresting the progress, and guarding against the occurrence, of that disease. We are thus forced to the conclusion that the curative effect of quinine in malarial fever is not to be explained by any action which that drug exercises on the system. The only alternative view is that it acts on the poison of intermittent fever, and deprives it of its power of affecting the system. That poison being a minute organism there is nothing improbable in the view that quinine should exercise a destructive action on it; for we know from the investigations of Binz that quinine possesses in a remarkable manner the power of destroying many minute organisms. It thus consists with both what we believe regarding the nature of malaria, and with what we know regarding the action of quinine on minute organisms, then quinine should possess the power of destroying that poison. The exercise of such a power over the malarial poison would amply explain both the prophylactic and curative actions of quinine in intermittent and remittent fever. And there is direct evidence that quinine does thus act on that poison; for in the course of the observations already referred to on Laveran's plasmodium malariæ it has been found that the effect of the administration of quinine is to destroy the parasite, or at least to make it disappear from the blood of a man in whose circulating fluid it was readily detected before the quinine was given. The plain inference is that quinine cures ague by destroying the parasite which causes it. The evidence in support of this view amounts almost to a demonstration that such is its mode of action. But, it may be said, if quinine owes its curative effects in intermittent and remittent fevers to its power of destroying minute organisms, why is it only in these maladies that this curative power is manifested? There are many other ailments which are believed to be produced in the same way, but in not one of them does quinine have the same power of arresting the morbid process.

In the natural history of minute organisms there is no fact better established than that such organisms are possessed of specific differences of whose existence their external form gives no evidence. Two

organisms may be indistinguishable from each other by the highest powers of the microscope—so far as can be made out by such examination they are identical, but it may be found by cultivation experiments that the one flourishes under conditions which are fatal to the other.

Again, an agency which destroys one such organism may have no effect on another. A remedy, therefore, which cures one disease by destroying the parasite which gives rise to it, does not necessarily cure all diseases owning a similar causation. Hence quinine may cure malarial fever by destroying the organism which produces it, without having a like destructive effect on the organisms which give rise to diphtheria, small-pox, scarlatina, typhoid fever, etc.

Minute organisms possessed of specific differences may have these differences manifested, not only by the different effects which they produce on the system, but by the different effects which other agencies have on them. The fact that quinine does not shorten the duration of all diseases caused by the propagation of minute organisms in the system, is no proof that it does not owe its power to cut short intermittent fever to a destructive action on the organism which gives rise to that malady. The fact that it does cut short this fever is to be accepted as a hopeful indication that other remedies may be found capable of exercising a similarly beneficial effect on other forms of fever whose course we are now powerless to control.

It is, indeed, in the recognition of this view—that the curative effect of a drug may be due to its action on the poison of the disease, rather than on the system in which it occurs, that lies the main hope for the future discovery of remedial agencies calculated to arrest the course of maladies which owe their causation to the propagation of minute organisms in the system.

One of the practical results of the study of the natural history of such organisms has been the recognition of the existence of agencies which exercise a destructive action on them. The recognition of such agencies, and of the possibility of dealing with diseased processes, and actually curing disease, by means of drugs which do not necessarily have any action on the system—which act not on the sufferer but on that which makes him suffer—the recognition of such a possibility marks an epoch in therapeutics and opens up a vast and interesting field of research. We know that the poisons which give rise to typhoid fever, scarlet fever, measles, and other allied maladies are minute organisms which are largely reproduced in the system during the course of the maladies to which they give rise, and whose morbific action is ultimately associated with their organic reproduction. The ideal method of treating these maladies, an ideal which may

some day be attained, would be to cure them by destroying the poison which gives rise to them, by administering to the sufferer something which, while it had no injurious effect on him, would kill the parasite which was making him ill. In malarial fevers the ideal is the same—only here it has been attained. That it has been attained in one disease should make us hopeful of getting like good results in others.

It was the belief (1) that the rheumatic poison was allied in nature to that of intermittent fever; (2) that both were minute organisms; (3) that the morbific effects of each were due to its propagation in the system; (4) that the curative effects of the cinchona compounds in intermittent fever were attributable to their destructive action on the poison of that disease—it was this belief that led to the inference that salicin might exercise a like destructive action on the poison of rheumatism.

If quinine destroyed the poison of intermittent fever, it seemed, for reasons already given, that salicin was not unlikely to exercise a like destructive action on that of rheumatism and a like curative effect on the disease to which it gave rise. That it does produce this curative effect has been abundantly demonstrated. All that has been said regarding the action of the cinchona compounds in ague is, *mutatis mutandis*, applicable to the action of the salicyl compounds in rheumatism. The analogies which are believed to exist between the poisons of intermittent and of rheumatic fever have already been pointed out. Between the cinchona compounds and the salicyl compounds there are also marked analogies.

1. The most prominent of these is the power which each possesses of curing a miasmatic fever. The cinchona compounds cure intermittent, the salicyl compounds cure rheumatic, fever.

2. The cinchona compounds are possessed of no physiological action by which their power to arrest the course of intermittent fever can be explained. It is the same with the salicyl compounds. On the non-febrile body they have no action by which their curative effects in rheumatic fever can be accounted for.

3. It has been hoped, and over and over again asserted, that salicin and salicylic acid possess a curative action in the same febrile ailments (typhoid fever, etc.), over whose course quinine was at one time believed to exercise a controlling influence. But the result has been the same as with the cinchona compounds. Though the salicyl compounds have been proved to be possessed of febrifuge properties they exercise no distinctly curative effect in any febrile ailment except acute rheumatism. As febrifuges they are much inferior to quinine. I have frequently seen a couple of ten-grain doses of quinine, given

the one an hour after the other, lower the temperature three or four degrees after several hourly thirty-grain doses of salicylate of soda had failed to have any effect.

But though the salicyl compounds possess the febrifuge property to a less extent than the cinchona compounds, they are not devoid of it. And we have now to inquire whether or not their beneficial action in acute rheumatism is due to this, or to some other special curative effect.

It is with the salicyl compounds in rheumatism as with the cinchona compounds in ague—there are but two ways in which their remedial action can be explained. Either they so act on the system as to render it insusceptible to the action of the rheumatic poison; or they so act on the rheumatic poison as to render it incapable of acting on the system. First as to their action on the system.

Like quinine the salicyl compounds have no effect on the temperature of the non-febrile body, but possess in an undoubted manner the power of lowering that of the febrile body. To produce this antipyretic effect they require to be given in much larger dose than quinine, and even then their action is less certain and less decided than that of the cinchona alkaloid.

Riess has maintained that salicylic acid shortens the duration of typhoid fever. I have given it freely in both typhus and typhoid fevers, and never found any evidence that it either shortened the duration or diminished the mortality of either of these maladies. This seems to be the experience of most observers. Were Riess right on this point, the accuracy of his statement would have been placed beyond doubt before now; for salicylic acid was freely used in typhoid fever before it was given in acute rheumatism. Its remedial power in rheumatism has been a matter of demonstration for years. Its remedial power in typhoid fever has never been demonstrated: and evidence is every day accumulating to show that Riess erred in attributing such an action to it.

Evidence all tends to show that though the salicyl compounds are possessed of undoubted febrifuge properties, there is but one febrile ailment in which they are known to exercise a distinctly curative effect. In other fevers they may for a time lower the temperature, but they do not materially alter the course or curtail the duration of the malady. In rheumatic fever alone they put a stop to all that constitutes the ailment.

But rheumatic fever does not consist solely of fever. An essential part of its existence is inflammation of the fibrous textures of the motor apparatus. Just as it is impossible for any poison to produce the disease without causing inflammation of these textures, so it

is impossible for any remedy to cure it without allaying that inflammation.

In considering the curative action of the salicyl compounds in this disease attention has been directed too much to the rapidity with which the temperature has been reduced and not enough to the equally great rapidity with which the joint inflammation is arrested. Indeed the arrest of this and the speedy relief of the suffering to which it gives rise constitute the most striking of the effects of the salicyl compounds in rheumatic fever. A man may be screaming with agony and unable to move arm or leg without the most acute suffering; the joints are swollen and inflamed, and his condition one of intense misery. Salicin or salicylic acid is administered in thirty-grain doses every hour, and in eight or ten hours the pain is gone, the joint inflammation is arrested, the man can move his limbs, and the joints can be handled without causing discomfort. No febrifuge action can explain this. No remedy which simply allayed fever could give such a result. In the whole field of practical medicine we know nothing like it. There is no other instance in which acute inflammation of any structure is arrested with the rapidity with which the salicyl compounds subdue acute rheumatic inflammation of the joints. And the joint inflammation of acute rheumatism is the only form of inflammation over which the salicyl compounds exercise this controlling influence. The curative effects are not due to their febrifuge properties; they are not due to any power of arresting the process of inflammation, and yet in acute rheumatism they rapidly subdue fever and arrest inflammation of the joints. They put a stop rapidly and effectually to the whole process of acute rheumatism, and they do this without having the power to arrest any other morbid process. Clearly their action is essentially anti-rheumatic. They act not on the system, not on the joint tissues, but on the rheumatic poison. The symptoms of acute rheumatism are all due to the propagation in the system of the organism which constitutes the poison of the disease; the salicyl compounds arrest these by destroying that poison. The rapidity with which the disease is arrested resembles the crisis of a fever more than anything else. The crisis of a fever means the cessation of the action of the poison which causes it. The rapid decline of the symptoms of acute rheumatism under the influence of the salicyl compounds means the same thing—the cessation of the action of the rheumatic poison. In both cases the cessation of the symptoms is somewhat abrupt—in the one case the poison ceases to be reproduced because the material necessary to its reproduction is exhausted; in the other the poison ceases to be reproduced because it is destroyed.

The Heart Complications of Rheumatism.

The cardiac apparatus is made up of the following structures

1. The hollow muscular substance of the heart, which by its contraction initiates the movement of the blood.

2. Rings of white fibrous tissue which surround and form the basis of the arterial and auriculo-ventricular openings, and to which the muscular fibres are attached.

3. Fibrinous valves whose structure is continuous with that of the rings, and whose function it is to close the various openings of the heart, to resist the backward tendency of the blood, and keep it in the proper channel.

4. A membrane which lines the interior of the heart's cavities, and is reflected over the fibrous structure of the valves, and whose smooth surface facilitates the onward flow of the blood.

5. An investing membrane which covers the heart externally, and whose peculiar formation and smooth glistening surface facilitate the free action of that organ.

All these structures, with the single exception of the internal lining membrane, find their analogues in those which go to form a complete and perfect joint. They are all apt to suffer in the course of acute rheumatism, though not all to the same extent.

The function of cardiac muscle, like that of voluntary, is to initiate movement. The function of the fibrous structures of the rings and valves, like that of the fibrous tendons and ligaments, is to afford attachment to muscle, and to regulate normal and prevent abnormal movement.

The function of the pericardium, like that of the synovial membrane of the large joints, is to facilitate free movements.

The endocardium alone has no analogue in the structures of a joint.

When considering the action of the rheumatic poison on the joints we saw that the structures which suffer most are the fibrous textures which regulate their movements—the ligaments and tendons. It is the same in the heart. The structures which chiefly suffer are those which regulate the movement of the blood, the fibrous rings, and valves.

It is its tendency to affect the heart that imparts to rheumatism its gravest features. In the majority of fatal cases death is attributable to some form of cardiac inflammation.

Bouillaud was the first who insisted on the essential nature of the connection between rheumatism and this inflammation. Its frequent

occurrence in the course of that disease had indeed been pointed out by others before him, notably by Pringle. But it is to this distinguished French physician that we must accord the credit of having first insisted on the frequency and true nature of the heart affection. Before his time it was looked upon as a sort of metastasis, or retrocession of the inflammation from the joints to the heart. He regarded it as "one of the elements of the disease," and as early as 1835 advocated the view, which has since been generally accepted, that pericarditis and endocarditis are of frequent occurrence in the course of acute rheumatism, and are to be regarded as produced in the same way as the joint inflammation.

In all forms of rheumatism, acute, subacute, and chronic, the heart is apt to suffer. In the acute the cardiac inflammation partakes of the generally acute character of the attack and the symptoms are well marked from the commencement. In the subacute the symptoms are less marked, and the immediate result of the cardiac mischief is less a source of anxiety. In the chronic its onset is so gradual that the cardiac affection seldom attracts attention until it is so far advanced as to cause serious disturbance of the heart's action, and the general symptoms of cardiac disease.

The exact proportion of cases of acute and subacute rheumatism during whose course recent cardiac inflammation occurs is differently stated by different observers. And the nature of the question is such that discrepancies must exist. In acute attacks the heart is more apt to suffer than in subacute, and young patients are more liable to this complication than more elderly ones. The acuteness of the attack and the age of the sufferer are thus important elements in determining whether or not cardiac complications are likely to occur. An observer the majority of whose cases are subacute, and the average age of whose patients is thirty, will have a smaller percentage of cardiac complications than one who happens to have a larger number of acute cases, and the average age of whose patients is twenty.

Fuller and others have endeavored in studying this question to distinguish between acute and subacute rheumatism. But independently of the difficulty, nay the impossibility, of drawing a distinct line of demarcation between them, there is no pathological reason for doing so. Acute and subacute rheumatism are merely different degrees of severity of the same disease. That the heart is more apt to suffer in acute cases is no doubt true, but this implies no pathological difference between them and subacute cases in which this tendency is less marked.

A study of the statistics bearing on this point leads to the conclusion that we are very near the truth when we say that, in the course

of acute and subacute rheumatism, recent cardiac inflammation occurs in about thirty per cent., or in nearly one case in three. But such a general statement is bald and to some extent misleading without the additional statement that as years advance the tendency to such complications diminishes.

Three facts are specially prominent in the history of rheumatic inflammation of the heart:

1. It is most common in young people;

2. It is more apt to occur in acute than in subacute cases of rheumatic fever;

3. It is limited to the left side of the heart.

No theory of rheumatism is satisfactory which does not explain these very striking facts.

1. *The Heart is Specially Apt to Suffer in Young People.*—This is a fact which has been observed and commented on by most writers on the subject. Dr. Peacock gave it as the result of his observations on 233 cases of acute and subacute rheumatism, that of those under twenty-one years of age 33.3 per cent. suffered from recent cardiac disease, while of those over forty only 16.6 so suffered; showing that the occurrence of cardiac complication is much more to be apprehended in young people than at more advanced ages. This accords with general experience. What is the explanation of it?

We have seen that rheumatism is essentially a disease of adolescence and early manhood, and that the textures which suffer most are the fibrous and serous tissues of the large joints. The tendency of a given portion of fibrous or serous tissues to be affected by the rheumatic poison is directly as its functional activity. Hence the tendency of the disease to attack the large joints. Adolescence and early manhood are the periods of life at which the functional activity of the textures which suffer is at its height; hence rheumatism is most common in young people. Applying the same reasoning to the case of the heart, we find in it an adequate explanation of the fact which we are now considering, that that organ is more apt to be the seat of recent rheumatic inflammation in young people than in those of more mature years. Muscular exertion increases the force and frequency of the heart's action. The more work the voluntary muscles are called upon to do, the greater is the demand for blood in them, and the greater the force and frequency of the heart's action. In other words, the voluntary muscles and the muscles of the heart work hand in hand; functional activity of the former necessitates functional activity of the latter. In this physiological fact we have the explanation of the pathological one which we are now considering. Rheumatism of the joints is most common in youth because youth is the

time at which these structures enjoy the highest degree of functional activity. Rheumatism of the heart is most common at the same age, and for the same reason. Sudden and rapid movements, involving correspondingly sudden and rapid increase in the force and frequency of the heart's action, are more frequent before than after the age of forty. Before that age the heart's structures are, therefore, subjected to greater and more frequent calls than they have to bear in more mature years, and must be ready to meet them. With the decreasing functional activity of advancing years comes also diminished susceptibility to the action of the rheumatic poison.

It is a *clinical* fact that the age of susceptibility to the action of the rheumatic poison is from fifteen to fifty. It is a *physiological* fact that the tissues on which that poison acts have a higher degree of functional activity during the earlier than during the later years of that period. It is a *pathological* fact that the tendency of a given portion of fibrous tissue to be affected by the rheumatic poison is directly as its functional activity. It follows that the textures of the heart ought to be more subject to rheumatic inflammation in youth than they are in more mature years. And all observation shows that they are so.

2. *Inflammation of the Cardiac Structures is more Common in Acute than in Subacute Attacks of Rheumatism.*—What is an acute, and what a subacute, attack?

An acute attack is one in which the rheumatic inflammation is both extensive and severe, affecting several joints and affecting them smartly. In other words, it is a rheumatic attack occurring in one in whom the rheumatic constitution is very marked, in the fibrous tissues of whose motor apparatus the nidus requisite to the reproduction and action of the rheumatic poison is abundantly and widely distributed, and on whom, therefore, that poison exercises a very decided action. The more abundant and wide the distribution of the nidus, the more likely is it to exist in the heart as well as in the joints, and the more likely is the heart to be affected. As a result of its abundance, the inflammation of the individual joints is severe; as a result of its wide distribution many joints suffer. There are fifteen common seats of rheumatic inflammation—fourteen in the joints and one in the heart. The wider the distribution of the nidus the larger the number of these seats likely to suffer at one time. In this respect the heart is in the same position as a joint; so that the wider and more abundant the distribution of the nidus the more likely is that organ to suffer. The same circumstances which make a rheumatic attack acute and severe tend also to give rise to heart complications, and thus is explained the fact that such complications are

more apt to occur in acute cases. The heart suffers in such cases for the same reason that a large number of joints do.

Given a severe and acute rheumatic attack during whose course ten of the fifteen common rheumatic centres are affected—the heart is more likely to be among the ten which suffer than among the five which escape; the chances are two to one against it. Given a mild and subacute attack during whose course only five centres are affected—the heart is more likely to be among the ten which escape than among the five which suffer; the chances are two to one in its favor.

The effect of age in increasing and diminishing the danger to the heart we have already considered. The influence of these two agencies, the age of the sufferer and the severity of the attack, ought to be considered conjointly; for severe attacks of acute rheumatism seldom occur except in youth; and nearly, if not quite, always in youth for the first time. It is probable that the severity of the attack has, in the manner just explained, as much to do with the production of the heart affection as has the youth of the sufferer.

The rheumatic constitution is not acquired, but natural—maybe inherited. A man who has it can scarcely reach the age of forty in a temperate climate without suffering from rheumatism; and he is more likely to suffer for the first time between the ages of twenty and thirty than between thirty and forty—and that simply because the former decade comes first. If his constitution be a markedly rheumatic one he will suffer severely, and the majority of his rheumatic centres will be affected. The heart is more likely to be in the majority which suffer, than in the minority which escape. That organ suffers, therefore, not so much because the man is young, as because his constitution is a markedly rheumatic one; and because exposure to the rheumatic poison is too common to permit of the likelihood of his getting beyond youth without suffering from its action.

That the rheumatic constitution is less marked after middle age has already been seen. This involves diminished susceptibility to the action of the rheumatic poison; and this is common to the whole of the structures affected in rheumatism, those of the heart as well as those of the joints.

3. *Rheumatic Inflammation of the Heart is Limited to the Left Side.*—In considering the action of the rheumatic poison on the joints we saw that those which suffer most are the ones which enjoy the highest degree of functional activity, and are habitually subject to free and active movement—the large joints. We find the same thing in the heart; the muscles, the valves, the fibrous rings, the lining and investing membranes are, as regards structure and function, the same on the right as on the left side; only those of the right side have a

less degree of functional activity; the muscular walls are thinner and less vigorous, and the valves contain less tendinous material. These structures are thinner and weaker on the right side because they have less work to do and less strain to bear. The difference between the two sides of the heart in this respect is evidenced by a reference to the contractile force of each ventricle. The walls of the left ventricle are much stronger and thicker than those of the right, "the proportion between them in this respect being as three to one" (Quain). It follows from this that the left ventricle acts with three times the force of the right; its fibrous structures and valves have therefore to bear three times as much strain, and enjoy a correspondingly higher degree of functional activity. "The work done by the right ventricle may be set down as one-third of that of the left" (McKendrick.)

The fibrous structures of the right side of the heart thus bear to those of the left the same relation that the fibrous structures of the small joints bear to those of the large; they have not the same degree of functional activity, are not called upon to do so much work, and are not a nidus for the rheumatic poison. The right side of the heart escapes for the same reason that the small joints do.

Rheumatic inflammation of the heart is generally described as occurring under the three forms of endocarditis, pericarditis, and myocarditis—inflammation of the lining membrane, inflammation of the investing membrane, and inflammation of the muscular substance. For clinical purposes this is as convenient a classification as could be adopted.

Endocarditis.

By the endocardium the anatomist means the thin transparent membrane which lines the interior of the cavities of the heart, is reflected over its valves and muscular folds, is continuous on the left side with the lining membranes of the aorta and of the pulmonary veins, and on the right with those of the pulmonary artery and systemic veins.

The clinical observer attaches to the term a wider meaning, and includes under it all the structures which lie inside the heart—the fibrous rings and valves as well as the lining membrane. It is of importance that this distinction should be borne in mind, for we shall presently see that the endocardium of the anatomist, the lining membrane of the heart properly so-called, is never the primary seat of rheumatic inflammation. We now use the term in its wider sense. By endocarditis we mean inflammation of any or all of the non-mus-

cular structures situated inside the heart—the fibrous texture of the rings and valves as well as the lining membrane.

Rheumatic inflammation never affects the whole surface of the lining membrane of the heart; it is limited to the part which is reflected over the valves; and when other parts suffer the mischief is almost invariably attributable to mechanical injury produced by the rubbing on the affected portion of the endocardial surface of an already damaged valvular segment. Moreover, the inflammation does not affect the whole valvular surface; only one side of a segment suffers—that, namely, which comes in contact with another segment in the act of closure—in the aortic valve its convex surface, and in the mitral its auricular. The damage is further limited in its early stage to the line at which the segments come into contact.

The limitation of the disease to this particular part of the valve has been attributed to the fact that it is the part which is most exposed to friction. "In its earliest stages it always occurs near the edges of a valve in the formation of a line of little elevations along the contact line of its segments, where the friction is greatest" (Wilks and Moxon).

"It is those portions of the valve which come into contact in the act of closure and are thus most exposed to friction, which are especially involved, and in which the changes usually commence" (T. Henry Green).

That friction may produce inflammation of the lining membrane of the heart there can be no doubt. Occurring in other than its valvular portion it is almost always due to the rubbing on its surface of a damaged valve. Knowing this to be the case, and finding that inflammation of its valvular portion commences at the line of contact of the different segments of the valves, and therefore at the point at which, if anywhere, they must rub, we cannot fail to see that there is good reason for the belief that friction plays an important part in the production of the inflammation of the lining membrane of the heart's cavities which is found in connection with acute rheumatism. Were this lesion the direct result of the action of the rheumatic poison it would not be limited to one side of the valve; it would affect both. Furthermore, its invariable limitation to the points at which the valvular segments come in contact shows that the cause which gives rise to it is something which comes into play only at that point. Friction is the most probable if not the only possible cause, and as the seat of the lesion is also the only point at which friction can come into play, the conclusion is forced upon us that friction is the direct cause of the lesion.

But the question arises—Why is there friction? Why do the

segments of the valves rub against each other? When a valve is already damaged or roughened, it is easy to see how further damage may be done; but in a smooth, uninjured valve how is the mischief set agoing? It cannot be that the valves constantly and and naturally rub against each other—for in that case, if friction produced endocarditis, no one would be free from it; rheumatic and non-rheumatic subjects would equally suffer, and a smooth, healthy valve would be the exception.

For the segments of the valves to come in contact is natural; but contact does not imply friction. Healthy valves normally come into firm and close contact, without in any way rubbing against and irritating each other; and this all the valves of the heart do seventy times every minute—100,800 times every day, 36,892,000 every year—and yet there is no evidence of friction or irritation until suddenly some day, after this smooth action has gone on uninterruptedly at this rate for maybe twenty-five years, and after the segments of each set of valves have, without injury and without rubbing, come into close and direct contact more than nine hundred millions of times (922,300,000) suddenly some day the rheumatic poison gains entrance to the system, and the smooth working of the valves comes to an end—they begin to rub; the friction gives rise to irritation and inflammation of the surface of the valve, and the symptoms and signs of endocarditis are developed. How is this? How can the rheumatic poison cause the segments of the valves to rub against and irritate each other? That they do rub is undoubted. That the rheumatic poison is the cause of the morbid change is equally undoubted. The question which we have to consider is how the friction is produced.

If the inflammation of the endocardial covering of the valve be the result of friction—and there is no reason to doubt that it is so; and if this friction be a result of the action of the rheumatic poison on the valve—and there is no reason to doubt that such is the case—there must be a stage of the valvular lesion which not only precedes the inflammation and roughening of its endocardial covering, but precedes and gives rise to the friction which causes this. Wherein does this stage consist?

Structurally a valve consists of two folds of the endocardium enclosing between them the fibrous or tendinous material which imparts to the valve its strength, its capacity to resist the pressure of the blood, and to perform the function which it is intended to fulfil. In endocarditis the inflammation must commence in one of these structures, for there is no other structure to be affected; and there is good reason to believe that the mischief commences in the fibrous structure of the valve and involves its endocardial covering only secondarily.

We have already seen that the rheumatic poison acts chiefly on those fibrous structures which enjoy the highest degree of functional activity. This is why the large joints suffer more than the small, and the valves of the left side of the heart rather than those of the right. The part of the valve which fits it for the work it has to do, and imparts to it its strength and capacity to resist pressure, is not the endocardial covering but the fibrous structures which that encloses. This fibrous structure is the seat of functional activity; for that reason it is the part of the valve on which we should expect the rheumatic poison to act primarily and chiefly. And so it is found to be. The stage of rheumatic endocarditis which not only precedes the evidence of inflammation of the endocardial covering of the valves, but also precedes and gives rise to the valvular friction which induces that inflammation, is the stage of inflammatory thickening of their subjacent fibrous texture. The earliest change which takes place in this texture as a result of the inflammation consists in multiplication of its cellular elements. This is the first and earliest result of the action of the rheumatic poison on the valve. Let us see how this would affect the aortic valve. A segment of this valve consists of a duplicature of the endocardial lining membrane, inclosing within it the fibrous structure. At the centre of its free border is an elevated fibro-cartilaginous nodule—the *corpus Arantii*. Bands of fibrous tissue stretch across the valve to its nodule from the border of valvular attachment to the aortic ring. Some of these run along its free surface; others spread out over the body of the valve, and come to a point, as it were, at the *corpus Arantii*. Between the fibres of the free margin and those of the body of the valve there is, on each side of the nodule, a small space over which no fibres run. This space, called the *lunula*, consists simply of a duplicature of the endocardial lining; it is the thinnest part of the valve. In the act of closure the three segments of the valve are thrown together into the middle of the aortic outlet, and the three *corpora Arantii* come into contact at its centre. The three lunulæ also come into contact, and are firmly pressed against each other by the aortic column of blood. They are all equally pressed down by this column; but the pressure thus exercised on each individual segment is counterbalanced by the counter-pressure on its other side of the two remaining segments. Thus this thin portion of the valve is freed from strain; for the greater the pressure of the blood column the more perfect is the contact of the lunulæ, and the greater the counter-support which they give each other. The part on which the strain falls is the thicker fibrous portion of the valve which bounds the lunula below. The strain begins where the counter-pressure of the opposing segments ceases. "The

force of the reflux is sustained by the stouter and more tendinous part of the valve" (Quain).

This stouter and more tendinous part it is which suffers in acute rheumatism. The lunula is not affected. The granulations which are formed on the surface of the endocardial lining in the earlier stage of inflammation of that membrane are limited to the convex surface of the line of fibrous tissue which passes from the attached border of the valve to the *corpus Arantii*, and which bounds the lunula below. Along this line the granulations run like a row of beads. The band of fibrous tissue which forms this line is at once the lowest part of the seat of valvular contact and the highest part of the seat of valvular strain. Above it there is no strain; below it there is no contact. It is the chief seat of functional activity, therefore its fibrous tissue is the seat of rheumatic inflammation; it is the lowest line of the seat of contact, therefore its endocardial covering is the seat of friction, when rendered unduly prominent by thickening of the subjacent fibrous tissue.

In the mitral valve there is no lunula; the whole structure is equally strained, and no one part is weaker than the rest. A weak point would be very liable to give way, for the strain on this valve is both greater, and more equally diffused over its surface, than is the strain on the aortic. In the case of the aortic valve there is only the blood pressure to be resisted; but in the case of the mitral there is both the blood pressure and the strain of the tightened chordæ tendineæ.

The fibrous structure of the whole valve may be the seat of inflammatory thickening; but the evidence of inflammatory change in its endocardial lining membrane is limited to the auricular surface, and to the line of contact of the valvular segments. In other words, in the mitral as in the aortic valve the granulations are formed at that line which is at once the seat of strain and the point of contact. It is the seat of strain, therefore its fibrous tissue is the seat of rheumatic inflammation. It is the point of contact, therefore its endocardial covering is the seat of friction when rendered unduly prominent by inflammatory thickening of the subjacent fibrous textures. Normally a valve is so perfectly adapted to the size of the orifice which it is intended to close, that in the act of closing its segments come into perfect and firm contact without any friction. They are firmly pressed against each other, but they do not rub. But if the segments be thickened, it is evident that they must come into contact sooner than they ought. The size of the orifice to be closed being unchanged and the force which closes it remaining the same, these thickened segments must come in contact before the closing force is

expended. The continued operation of that force after the segments of the valve are in full contact, must lead to further movement of the segments. Normally their movement is completed at the moment of perfect and close contact; but with a thickened valve contact takes place too soon, and movement is continued for an appreciable time after that event—with the necessary result of causing the valvular segments to rub against each other at the point of premature contact.

To put it otherwise: The swelling of the deeper fibrous textures of the valves necessarily elevates and makes more prominent the superficial covering of the swollen part. As the segments of the valve close, the unnaturally prominent endocardial covering of each comes into abnormally early contact with the opposing segment. The continuance of the act of closure, and therefore of valvular movement, after such contact is complete necessarily causes these elevated surfaces to rub against each other. This friction produces irritation and inflammation of the endocardial coating of the valves at their line of contact. The point is that the primary action of the rheumatic poison on the valves is to cause thickening of their deeper fibrous structure, and that the roughening of the endocardial surface is a secondary consequence of this, and not a direct result of the action of the rheumatic poison on it.

The morbid changes which take place in acute rheumatic endocarditis are as follows:

1. There is multiplication of the cellular elements of the fibrous structure of the valve;
2. As a consequence of this these fibrous structures are thickened;
3. As a result of this thickening there is undue prominence of the endocardial covering of the valve;
4. As a consequence of this the surfaces of the valvular segments come into abnormally early contact in the act of closure;
5. This causes them to rub against each other during the latter stage of this act;
6. The friction thus produced causes irritation and roughening of the surface of these valvular segments at the point at which they rub;
7. This roughening it is which produces the physical signs of endocarditis.

It will be seen from this that the changes in the endocardial lining membrane by which we diagnose endocarditis are a comparatively late stage of the disease, and that the earlier changes in the valve give rise to no physical signs and cannot be diagnosed—an important point to bear in mind when considering the action, curative and prophylactic, of remedial agents.

Microscopic examination of the affected portion of valve confirms

this view of the nature and seat of the morbid change. On making a section of one of these granular nodules, and submitting it to such examination, it is found that the seat of swelling is the deep layer of fibrous tissue, and that the superficial lining of the valve is merely raised up by the multiplication of the cellular elements of the subjacent fibrous texture. "If a valve with these nodules be cut for the microscope across the plane of its curtain, so as to show a section down through one of the small nodules, this will be found to be composed of a simple cloudy swelling of the tissue of the valve through a multiplication of the cellular elements in its fibrous structure, which here and there by its excess raises the surface into a little hillock. If the hillock takes the form of a distinct projecting grain, you will always find on the top of it a cap of fibrin separated from its substance by a line which the microscope defines very clearly. This cap of fibrin differs in composition from the hillock itself, though the difference is more easily seen than described, for the organization in both is very low; but the fibrin is almost structureless, while the hillock of swollen valve substance shows the regularly placed nuclei of fibrous tissue" (Wilks and Moxon).

The cap of fibrin here described is fibrin which is deposited directly from the blood on the roughened surface of the endocardium, just as it would be deposited around any foreign body. The true seat of the inflammation is the deeper fibrous tissue of the valve.

When rheumatic inflammation attacks the fibrous rings it produces there the same multiplication of the cellular elements and the same thickening as it causes in the valves, but thickening of the fibrous textures of the rings is not of so much importance, for it gives rise to no such rubbing as takes place when the valves are affected. The sole result is thickening of the fibrous rings, and possibly some narrowing of the orifice. There is no friction, and no roughening of the endocardial surface.

Rheumatic endocarditis then is primarily and essentially a disease of the fibrous structures of the heart. It is therefore limited to that portion of the endocardial contents in which these structures exist. The small portion of the lining membrane of the heart which covers the fibrous valves very frequently suffers; the much more extensive portion which lines the heart's cavities remains unaffected. The sole difference between the two is that the one is, and the other is not, in direct contact with the fibrous textures, and that the one is, and the other is not, the seat of friction when these textures are inflamed and swollen.

The lining membrane of the heart differs in structure, in nature, and in function, from that which invests it externally. Error and

misconception have arisen from not recognizing this, and from regarding endocarditis as bearing to the endocardial lining membrane the same relation that pericarditis bears to the pericardial investment. There is little or no analogy, either physiological or pathological, between the two membranes. The function of the endocardial lining is, by presenting a smooth surface to the blood, to facilitate its onward flow. It has exactly the same part to perform as the lining membrane of the great vessels, with which it is structurally continuous. Neither in the heart nor in the arteries does this membrane tend to take on inflammatory action; and when inflammation does occur in it, it shows no tendency to spread. The irritation produced by the rubbing of a valvular vegetation against the lining membrane of the ventricle may be so great as to cause ulceration at the point of contact; but the mischief is limited to this point, and does not spread. There is no such disease as acute general rheumatic inflammation of the endocardium. The membrane has no vessels, and inflammation cannot spread over its surface, as it does over that of the vascular pericardium.

The symptoms and signs of rheumatic endocarditis vary with the seat of the disease and the severity of the attack. Occurring as it does in the course of acute rheumatism, any febrile disturbance to which it may give rise is apt to be lost in that attributable to the joint inflammation. That endocarditis slightly raises the temperature there can be no doubt, but the invasion of fresh joints has a more marked effect in that way, and as the cardiac complications generally occur at a stage of the illness when fresh joints are apt to suffer, it is seldom possible to say how much of the abnormal rise is due to the heart affection. Inflammation of the endocardium may cause less general disturbance than inflammation of a joint, while its local effects may be so slight as to cause no discomfort to the patient.

The symptoms special to it are subjective and objective. The subjective are not commensurate with the serious nature of the ailment. They vary with the severity of the attack. Frequently they are altogether absent. In very acute cases there may be pain in the cardiac region; the heart's action may be disturbed and rapid, the breathing accelerated, oppressed, or even labored, and the patient very anxious. If both aortic and mitral orifices and valves are acutely inflamed, such are apt to be the symptoms. But in such acute cases the muscular substance of the heart is generally more or less involved in the inflammatory mischief, and it is probable that some of the symptoms are due to this, as much as to the endocardial inflammation. Moreover, the pericardium is also liable to be inflamed in such severe cases.

When the inflammation is less severe and is limited to the endocardium there may be little or no disturbance of the breathing or of the cardiac action. In many cases subjective symptoms are entirely absent; and the sole indication of the existence of the endocarditis is the altered character of the heart's sounds, the alteration generally consisting in the development of one or more murmurs.

It has been said that such murmurs may be of anæmic origin. I do not think that nowadays they ever are so. They may sometimes have been so in the old days of free bleeding: but in the absence of such treatment it is scarcely possible for an anæmic murmur to be developed in the short time that suffices for the production of those which we are now considering. In acute rheumatism an anæmic murmur could scarcely be developed till late in the case: those now under consideration generally appear in the early stage of the disease.

In the aortic valve we have seen that the morbid change consists in the thickening of its segments, and in roughening of their convex surfaces. During the systole of the heart these segments are thrown against the walls of the aortic outlet. Thickening of their fibrous texture must, therefore, cause a diminution of the calibre of this outlet—a diminution which is directly as the extent of the morbid change; while the deposition of fibrin on the surface of the valve not only further diminishes the aortic outlet, but, by presenting to the blood a roughened surface, interferes with the naturally smooth and easy passage of that fluid from the heart into the great vessels. The result and the physical evidence of this state of matters is the development of a systolic murmur loudest at the base, and transmitted into the aorta. If one or more of these segments should be so altered as to render due closure of the valve impossible, some of the blood regurgitates back into the ventricle from the aorta, and there is developed a diastolic murmur transmitted downward into the heart and most distinct at mid-sternal region.

Thickening of the fibrous structures of the heart is not limited to their valvular portion: the rings also suffer. The effect of this on the aortic ring is still further to diminish the calibre of its outlet and increase the signs of aortic obstruction.

In the mitral valve the morbid change consists in thickening of its structure, and in roughening of its auricular surface at the line of contact of its segments.

Such morbid change in the mitral valve is apt to produce more serious disturbance of the valvular function than does a corresponding change in the aortic. For in the aortic the thickening is partial; the lunulæ are not affected, and so long as they come well into contact the valve continues to perform its function. But in the mitral

valve there is no lunula; the whole segment is thickened. This means loss of mobility, loss of pliability, and consequent loss of adaptability—a condition which is exaggerated by the roughening of the surface of the valvular segments at their line of contact. The result is that the two segments do not come into close and perfect contact, a certain quantity of blood regurgitates back into the auricle, and there is developed a mitral systolic murmur.

Should the fibrous ring be sufficiently thickened to cause any narrowing of the mitral orifice there will be developed a presystolic blow—the evidence of mitral obstruction.

Thickening of the rings gives rise to no friction and no roughening of the endocardial surface, and is for this reason more often recovered from than thickening of a valve.

The absence of pain in rheumatic inflammation of the fibrous textures of the heart is one of the chief points of distinction between it and similar inflammation of the fibrous textures of the joints. Another distinction, and one of much more serious import, is that the results of rheumatic inflammation of the textures of a joint are generally transient and perfectly recovered from; while those of like inflammation in the textures of the heart are apt to be permanent. Why is this? The poison which produces the inflammation is the same in both; its mode of action is the same; the tissue on which it acts has in each the same structure, and a similar function. Why, then, should the results be so different? The temporary character of the injury to the textures of the joints has been ascribed to the absorbent effects of the pressure exercised on the effused products by the surrounding solid structures. The permanence of the damage to the textures of the heart has been ascribed to the absence of such pressure. "The permanence of the injury in the case of endocarditis is simply due to the want of counter-pressure. In the joints the swollen membranes are pressed against the other solid structures as soon as the liquid effusion is removed. This pressure causes absorption of all the new products, whereas in the heart there is no direct pressure of solids against the inflamed valves, which stand freely in fluid blood, so that the new products persist" (Wilks and Moxon).

A more simple and adequate explanation of this unfortunate difference is to be found in the fact that when the fibrous textures of a joint are inflamed they get perfect rest, and are thus placed in circumstances favorable to complete recovery: while the fibrous textures of the heart not only get no rest, but, from the greater frequency of the heart's action, are called upon to do an increased amount of work. They are thus placed in circumstances which make complete recovery all but impossible.

Acute cases of rheumatism, in which the textures of the joints are smartly inflamed, in which there is a considerable amount of thickening and effusion, and in which complete rest is given to the inflamed textures, are also those in which these textures are most fully and speedily restored to their natural state. In chronic cases in which the inflammation is slight, in which the patient continues to go about, and in which the inflamed ligaments and tendons do not get rest, these textures are more apt to be permanently thickened. If pressure were the agency which removed the effusion, it ought to disappear more speedily in these chronic cases than in the acute; for the act of locomotion supplies this factor, and would lead to speedy absorption of the effused products, and early restoration of the fibrous textures to their normal state. The long duration of the thickening and stiffness of the joints in such cases is to be explained in the same way as the persistent nature of the cardiac damage. Absence of rest leads to imperfect recovery and permanent injury.

It is difficult for a heart whose fibrous textures have once been thickened by inflammation, and still more so for one whose endocardial lining has once been roughened, to recover its normal condition; for the fibrous textures continue to be strained, and the roughened surfaces of the segments go on rubbing. Irritation is thus kept up after the primary inflammation has disappeared: the thickening of the fibrous textures becomes chronic, and fresh rheumatic attacks are apt to add to the mischief. With the advance of time the morbid change is apt to become more marked, the valvular segments to become contracted and misshapen, the cardiac circulation to be more disturbed, the muscular walls of the heart to hypertrophy, and its cavities to dilate; and so the sufferer enters on a prolonged course of misery whose only termination is death.

It seems a simple statement of fact, clinical and pathological, to say that in rheumatic arthritis complete recovery is the rule, while in rheumatic endocarditis complete recovery is the exception. The statement is one which nearly every physician would indorse. Nevertheless it is not strictly accurate. It is bald, and misleading from its baldness. Everything which recovers in a joint may, and frequently does, recover in the heart. The structure in the heart which is apt to be permanently damaged is the endocardial lining, and this is the one structure which has no analogue in a joint. The pericardium corresponds in structure and function to the synovial membrane. The muscles of the heart have their analogue in the muscles of the limbs: the fibrous structure of the rings and valves resemble in structure and function the fibrous tendons and ligaments. The endocardium alone has no analogue in a joint; there is absolutely nothing

in or about a joint which at all resembles it either in structure or function. Anatomically it is continuous with the lining membrane of the great vessels with which, and with which alone, it has structural and functional affinities. The changes which take place in it during the course of acute rheumatism do not result from the direct action on it of the rheumatic poison, but are produced by rubbing of the valvular segments consequent on rheumatic inflammation and thickening of the subjacent fibrous structure of the valves.

The difference in the ultimate results of rheumatic arthritis and rheumatic endocarditis is to be explained in two ways:

1. An inflamed joint gets complete rest, and is thus placed under conditions most favorable to recovery. An inflamed heart not only gets no rest, but beats more quickly than natural.

2. The structure in the heart which is the chief seat of permanent damage, the endocardium, is one which does not exist in a joint, and bears no resemblance to anything that does.

Pericarditis.

Between the pericardium of the Anatomist and that of the Pathologist there is no difference. Rheumatic pericarditis consists in rheumatic inflammation of the investing membrane of the heart. As already explained, such inflammation is most common in acute cases and in young subjects.

Of all the serous membranes of the body the pericardium is the only one which invests an organ having free and active movements. So far as functional activity is concerned the pericardium is as much above other serous membranes, as the valves of the left side of the heart are above those of the right, and the fibrous tissues and serous linings of the large joints above those of the small. In its liability to rheumatic inflammation the pericardium is in the same position as the lining membrane of a large joint.

Pericarditis occurs in different degrees of severity. The whole membrane may be the seat of acute inflammation; or only a small part of it may be affected. According to its extent and severity are the symptoms to which it gives rise. As a rule, subjective symptoms are more marked than in endocarditis. In acute and severe cases pain in the region of the heart is generally present at the outset, and is often the first thing complained of. Usually it is increased by pressure over the heart, or in the epigastrium. The patient is restless and distressed; his countenance has an anxious expression; the breathing is quickened; there is generally a short, frequent cough; the heart's action is vigorous and rapid—may be tumultuous, vio-

lent, and irregular. On auscultation there is heard the friction sound produced by the rubbing against each other of the roughened pericardial surfaces.

But the heart symptoms are not always so distinct in these acute cases. Occasionally their place is taken by nervous symptoms so marked that the case is apt to be mistaken for one of cerebral rheumatism. The onset of the pericardial inflammation may be ushered in by delirium; and delirium, stupor, and coma may remain the characteristic symptoms throughout. From beginning to end there may not be a single subjective symptom of cardiac disturbance.

The following case, recorded by Andral, is a good illustration of the manner in which acute pericarditis may simulate inflammatory mischief in the nervous centres:

Case XI. "Symptoms of meningitis. Acute inflammation of the pericardium.—A woman, aged 26, the mother of two children, and who had recently had a miscarriage, was admitted into La Charité early in the year 1820, in such a state of delirium that no information could be got regarding her antecedents. The delirium was remarkable for the obstinate taciturnity by which it was accompanied. When asked a question, the patient looked fixedly at one without answering; the face was pale; the lips, separated from each other, and agitated from time to time as by a convulsive trembling, allowed the tongue to be seen, moist and white. The pulse was frequent and small, but regular; the skin rather cold.

"During the next two days there was frequent bending backward of the head, sudden raising of the trunk at intervals, and *subsultus tendinum*. The patient spoke, and appeared to understand what was said to her, but was quite incoherent in what she said. The face was very pale; the pulse very frequent, and intermittent. On the fourth day after admission the delirium ceased: the patient complained only of great weakness: the muscles of the face were agitated by almost continual convulsive movements; and the upper extremities were affected from time to time with an almost tetanic rigidity. On the fifth day the delirium returned, the features were distorted; during the course of the day the patient became comatose, and died in the evening."

On post-mortem examination it was found that "there was no appreciable change in the color or consistence of the brain, spinal cord, or their membrane. The digestive canal, opened throughout its whole extent, presented only a slight injection here and there. The other abdominal viscera were free from lesion. The lungs were slightly congested posteriorly. The substance of the heart presented no trace of morbid change: the vessels entering and issuing from it were also healthy. But the pericardium was covered with a lymphy deposit (*par des concrétions albumineuses*), which stretched at many points like a soft bridle from the visceral to the parietal surface. Effused into its cavity, too, were several ounces of a greenish and flocculent serum."

In subacute pericarditis the subjective symptoms are less marked. There may be no more than a sense of uneasiness about the heart, with some increased rapidity of its action.

In mild cases there may be no subjective symptoms whatever—nothing but the pericardial rub to point out the existence of the disease. In not a few such cases the inflammation is limited to that portion of the membrane which surrounds the great vessels at the base of the heart, and may give rise to no symptoms during life. In the post-mortem room this very limited form of the malady is often found in those who have died of some other complication. Not unlikely it is an extension to the pericardium of inflammation originating in the subjacent fibrous rings.

The earliest stage of acute inflammation of the pericardium consists in hyperæmia of the membrane. It cannot be said that this stage has any specially characteristic symptoms or physical signs. But in very acute cases it may be accompanied by increased vigor and energy of the heart's action. Without producing any *bruit* this increased vigor imparts to the first sound of the heart an exaggerated ring or tone, which may be sufficiently marked to enable us to suspect, if not actually diagnose, commencing inflammation of the pericardium. This "tension sound," as it has been called, may be regarded as the earliest objective evidence of the onset of pericarditis. It is only in acute cases that it is observed: and in them the first stage of the disease, during which alone it is heard, lasts for so short a time that this sign readily escapes detection. When observed, it is soon thrown into the background by the more striking and important indications of the following stage.

The second stage comes in quick succession to the first. It is characterized by the effusion of lymph, and the formation of a fibrinous layer of new material on the surface of the inflamed membrane.

It is at this period that the signs and symptoms of the disease come to the front, and that its existence is generally diagnosed. The new material which is formed on the surface of the pericardium produces a marked alteration there. Instead of a smooth glistening surface allowing the visceral to glide gently and easily over the parietal portion of the membrane, there is a coating of lymph which is so soft that its surface gets roughened by the rubbing to which it is subjected, and becomes more or less ragged and shaggy in appearance. The rubbing against each other of the thus roughened surfaces of the pericardium produces the "to and fro" friction sound characteristic of the disease. This sound is generally double, but may be single, and then is usually short, and may be with difficulty distinguished from an endocardial blow. It is generally heard first near the base of the

heart, but it may be distinct over the whole organ. It is superficial in character, like a pleuritic rub, but easily distinguished from that by its situation, and by its being independent of the respiratory movements. There is no increase of cardiac dulness. This is the stage at which any subjective symptoms which may exist are usually felt.

The morbid process may go no further than this. The inflammation may decline, the lymph may be reabsorbed, and the pericardium be restored to its natural state; or the two roughened surfaces may adhere together to a greater or less extent.

In acute cases there is generally a third stage, characterized by the effusion of serum into the sac of the pericardium. A certain amount of fluid is thrown out during the second stage at the same time as the lymph. The quantity may be so small that it gives no physical evidence of its existence, and is quickly absorbed when the inflammation subsides. The presence of a larger quantity gives very decided evidence of its existence. It separates the visceral from the parietal layer of the pericardium. Rubbing of the surfaces against each other thus becomes impossible, friction ceases to be heard, and any pain which there may have been disappears. The area of cardiac dulness is increased. If the sac of the pericardium be quite full, the region of dulness has the triangular shape of that sac—with the apex above and the base below. The dulness extends to the left of and beyond the apex point. The heart's impulse is not felt as in hypertrophy of the organ. The sounds are distant and indistinct. The pulse is quick and feeble—may be irregular. There is increased frequency of respiration, and the patient may be in considerable distress.

Under proper treatment, and in the absence of other complications, the fluid is generally absorbed. As it diminishes in quantity, the region of cardiac dulness also decreases. The two layers of the still roughened pericardium once more come into contact, and friction may be again heard for a day or two. Here, as in the case in which recovery takes place at the end of the second stage, the friction gradually disappears, and ultimately everything seems to return to its natural state, recovery being apparently perfect. It is doubtful, however, if the pericardium ever quite regains its natural condition. It may possibly do so in some cases; but in most instances more or less extensive adhesions are formed between its two layers. Where the inflammation has been severe, such adhesions are formed over the whole surface of the heart, and the sac of the pericardium is obliterated.

Such obliteration has been regarded by some as a source of much

embarrassment to the heart's action, and a cause of hypertrophy and dilatation of that organ. By others it has been said to produce some degree of atrophy of the heart; while a third set of observers maintain that an adherent pericardium gives rise to no symptoms during life, and to no morbid change in the muscular substance of the heart.

It is probable that the age and mode of life of the patient have much to do with the variety of the results noted by different observers. In young and excitable persons, and in those whose habits or tastes lead them to take much exercise, obliteration of the pericardial sac will cause inconvenience. The function of the pericardium is to provide for the free and active movements of special occasions and unusual efforts. If such occasions do not arise, and such efforts are not made, the obliteration of its sac causes no embarrassment, and no change in the heart. The ordinary work of that organ can be quite well done without the pericardium; and so long as this work is not unduly increased, and extraordinary efforts are not required, no harm results from the obliteration of its sac. It is for the free movements of special occasions that it is required.

There is one fact in the history of rheumatic pericarditis which has a most important bearing on the pathogenesis of the disease. This fact is that the disease almost always commences in the visceral layer of the pericardium and at the base of the heart.

The evidence of this is as follows:

1. In slight and circumscribed attacks, the inflammatory change is, as a rule, confined to this portion. Affecting only the visceral layer, and only a small part of it, there may be no physical signs or symptoms by which its existence may be diagnosed. But we know that such slight attacks do occur: for in the post-mortem room it is not uncommon to find some thickening and opacity, the result of inflammation of this part of the pericardium, without any other evidence of the disease having existed.

2. In cases in which the disease spreads over the body of the heart, and affects both layers of the pericardium, the friction sound is generally heard first near the base.

3. In cases in which death takes place in the early stage of the disease, it is found that while that part of the membrane which is situate over the body and apex of the heart is merely hyperæmic—is still in the first stage of inflammation—that which surrounds the origin of the great vessels at the base has reached the second stage, and is covered with shreds of lymph. "In ordinary acute pericarditis the earliest stage is seen as a minute injection of its vessels, causing a blush of redness, which close observation resolves into a beautiful red network. This injection is almost a certain proof of

pericarditis, but when you see it you should look at the base of the heart about the great vessels, where you will always find some shreds of inflammatory lymph" (Wilks and Moxon).

Is there any possible explanation of these facts—any reason why the rheumatic poison should act primarily and chiefly on this part of the pericardium? There is no structural peculiarity to account for it. It cannot be due to greater functional activity; for movement is freer at the apex than at the base. The only peculiarity of that portion of the pericardium which seems specially liable to rheumatic inflammation, is that it is situate over and in near contact with the fibrous textures of the heart—in near contact, that is, with that particular portion of the cardiac structures which is specially liable to suffer from the action of the rheumatic poison. The inference is inevitable that inflammation of the pericardium may, sometimes at least, be due not to the direct action of the rheumatic poison on that membrane, but to the extension to it of an inflammatory process originating in the subjacent fibrous textures. We have already seen that inflammation of the inner lining membrane of the heart is limited to that part of it which is in direct relation with the fibrous rings and valves, and is secondary to inflammatory change in these structures. There is not a little evidence to show that in many cases inflammation of its outer investing membrane has primarily a like limitation and a similar pathology.

When considering the pathogenesis of the joint troubles of acute rheumatism we saw good reason to think that inflammation of the synovial membrane was secondary to inflammation of the ligaments and tendons. There is equally good reason to believe that inflammation may in like manner extend to the pericardium from the fibrous textures of the heart; and that to such extension rather than to the direct action of the rheumatic poison on that membrane many cases of pericarditis are due.

Myocarditis.

When considering the question of the action of the rheumatic poison on the various structures involved in acute rheumatism, we saw good reason to believe that the voluntary muscles were directly affected by it, and that the excess of lactic acid characteristic of the disease was a consequence of increased muscle metabolism. If the voluntary muscles are thus affected, there is no reason why the cardiac muscles should escape, for they are similar in structure and function. Indeed in their case there is distinct and direct evidence that they do thus suffer during the course of rheumatic fever, for many cases have been recorded in which the cardiac walls have been found

after death to be the seat of inflammatory softening or induration. With this evidence of myocarditis there have usually been associated the ordinary post-mortem signs of endocarditis, of pericarditis, or of both. The existence of this association, and the rarity of post-mortem evidence of myocarditis except in combination with inflammation of the membranes, have not unnaturally led to the belief that inflammation of the muscular substance is secondary to that of the membranes, and results from the direct extension to it of an already existing inflammation of one or both of these.

Myocarditis occurring independently of endo-pericarditis is described by Walshe as "an affection, to say the least, of extreme rarity."

Peacock says that myocarditis "is rather interesting in a pathological point of view than practically important. It probably always occurs in connection with one or both the other forms of disease," *i.e.*, endocarditis or pericarditis.

"Inflammation of the heart substance is frequently set up in the layers contiguous to an inflamed endocardium or pericardium" (Roberts).

"Inflammation of the muscular substance of the heart rarely occurs except in connection with peri- or endo-carditis. In pericarditis a greater or less thickness of the muscular walls in contact with the inflamed serous membrane is often distinctly implicated; and there is no doubt that their inner aspect may be similarly involved during the course of an attack of endocarditis" (Bristowe).

But when we come to examine the grounds on which this opinion is based, we find that they are scarcely adequate to its support, and that especially the view that myocarditis is secondary to and dependent on prior inflammation of the endocardium is one which can hardly be maintained. The lining membrane of the heart is a non-vascular structure in which inflammation cannot, and as a matter of fact does not, spread. The morbid change which takes place in it during the course of acute rheumatism is secondary to change in the subjacent fibrous tissue, and is limited entirely to that part of the membrane which is reflected over the fibrous valves. It never extends to the much more extensive portion which lines and is in contact with the muscular substance, and from which alone it could extend to that substance. Limited as the morbid process thus is, showing no tendency to spread, and never affecting the part of the membrane which is in contact with the muscular walls, it is simply impossible that inflammation should extend from the endocardium to the muscular substance of the heart. Endocarditis and myocarditis may coexist, but myocarditis cannot be secondary to and consequent on endocarditis.

It is different with the pericardium: it is a very vascular membrane in which inflammation rapidly spreads; the whole membrane may suffer, and its inflamed part be in direct contact with the muscular walls. It is quite possible, therefore, that inflammation may extend from it to them; it is equally possible that the process may occasionally be reversed and that inflammation may extend from the muscular walls to the pericardium. But more probable than either is it that when pericarditis and myocarditis coexist, each occurs independently of the other—both being part of a general carditis.

The part of the heart which most suffers in rheumatic fever is the fibrous structure of the rings and valves. We have seen that inflammation of the endocardial lining is always secondary to a prior inflammation of the fibrous structure of a valve; and that there is good reason to believe that in many cases of pericarditis the inflammation spreads to that membrane from the fibrous structures at the base of the heart. If inflammation spreads from these structures to the endocardium and the pericardium there is no reason why its hould not equally extend to the muscular substance. There is every facility for its doing so, for the muscles of the heart are attached to the fibrous rings, and there can be little doubt that many cases of partial myocarditis in which the inflammation is limited to the base of the heart are so produced.

Rheumatic myocarditis, like rheumatic endocarditis, is almost entirely confined to the left ventricle, and for the same reason. It may be partial or general—involving a part, or implicating the whole structure of the muscular wall. The partial is the more common. Its situation is the base of the ventricle. It is probably due in most if not in all cases to an extension to the muscles of a prior inflammation of the fibrous structures. As there is usually a similar extension of that process to the endocardial lining, any symptoms to which the myocarditis might give rise are apt to be lost in the more obvious indications of the endocarditis. The evidence of its occurrence is found in the post-mortem room in the form of circumscribed patches of induration of the muscular walls of the ventricle, chiefly at the base and generally in company with thickening and induration of the fibrous rings and valves.

General rheumatic inflammation of the walls of the left ventricle, like other local inflammations, occurs in varying degrees of severity. When very acute, it may give rise to such destructive change in the ventricular walls that recovery is impossible. In a less severe form it causes simply softening of the ventricular walls—a condition which may be perfectly recovered from, or may result in more or less indu-

ration of the muscular substance; but which may also be a cause of sudden death.

Myocarditis is a formidable disease, apt to be fatal, and apt to be overlooked. It is apt to be fatal, because of the importance of the tissue inflamed; it is apt to be overlooked, because of the obscure and even misleading character of some of its most common and prominent symptoms.

Corvisart divided cases of myocarditis into two classes, the *distinct* and the *latent*—those in which the symptoms clearly indicate the nature of the disease and those in which symptoms directly referable to the heart scarcely exist.

Acute pain in the epigastrium, or præcordial anguish, a sense of oppression and anxiety, embarrassed respiration, the evidence of defective aeration of the blood, without any pulmonary lesion to account for it—such are the symptoms which may present themselves in distinct cases of acute myocarditis. Seldom, if ever, do they all exist at the same time. Now one, now another predominates. The most common are præcordial uneasiness, and evidence of defective aeration of the blood. With these there are associated symptoms of disturbance of the sensorium.

Myocarditis is often accompanied by inflammation of the endocardium or pericardium, or both. It is then part of a general carditis. The physical signs of the membranous inflammation are so obvious, that all the symptoms are apt to be ascribed to it. It is probable that the less obvious myocarditis plays a not unimportant part in the production of many of them: but how much of the patient's disturbance is due to the membranous and how much to the muscular inflammation it is impossible to say. It is a matter of course that when both the walls of the ventricle and the membranes are inflamed, there is likely to be greater disturbance and irregularity of the heart's action and a greater tendency to death, than when the membranes only are involved. But it is impossible to diagnose the extent of the myocarditis as we do that of the endo-pericarditis. All that we can say is that, if in the course of a case of rheumatic inflammation of the membranes, we find either a marked degree of cerebral disturbance without hyperpyrexia, or evidence of defective blood purification without any pulmonary lesion, or any serious amount of pericardial effusion, we may feel sure that the muscular substance of the heart is seriously involved in the mischief.

The physical signs of the membranous inflammation so predominate over any change in the cardiac sounds to which the myocarditis could give rise, that we can better diagnose the existence and gauge

the extent of this latter by a careful observation of the general symptoms, than by a physical examination of the heart.

There are cases of acute myocarditis, as of acute pericarditis, which run their whole course to a fatal termination without any symptom directly referable to the heart; the only symptoms being those of cerebral disturbance. An admirable illustration of this is found in a case recorded by Mr. Stanley in the seventh volume of the Medico-Chirurgical Transactions, 1816. So far as I know, it is the earliest recorded case of the kind.

Case XII.—"A boy, aged 12 years, although of a delicate frame, had enjoyed generally a good state of health. On Saturday, the 20th of April, he was apparently quite well, having been on that day on a visit to one of his relations by whom this remark was made. On the next morning he was brought to the Infirmary, discovering at that time the usual symptoms of fever, namely, great bodily heat, a quick pulse, the tongue white and much furred. On the next day (Monday), his fever was much increased, but the only pain of which he complained was in the left thigh and knee, which ceased before night; in the afternoon he became delirious with much watchfulness. On Tuesday the delirium was very considerable, but without any comatose tendency: the pupil of the eye much dilated, but not insensible to light. He complained but little of pain, but when closely pressed upon the subject he pointed to his forehead. Early in the afternoon of that day he had a convulsive fit which soon went off. In the evening all his symptoms became aggravated, and he passed the night almost without sleep. On the following morning he appeared much sunk; his breathing for the first time became difficult. He was then sufficiently sensible to answer any question put to him, but soon afterward he became insensible, and gradually declined till about two in the afternoon, when he expired."

Those who saw this boy thought that his symptoms were of cerebral origin, and "that there was effusion within the head."

The idea of there being anything the matter with the heart did not suggest itself to his attendants: and "at no period of his illness did he complain of pain in any part of the thorax, nor was there any irregularity, either in the action of the heart or pulsation of the arteries."

It having been considered from the general character of the symptoms that the cause of death was to be sought in the head, this was the part first inspected: "but after an attentive examination of the brain, nothing farther could be remarked than that the vessels were generally turgid; not more so, however, than is frequently seen when death has taken place under circumstances that lead to no suspicion of affection of the head." The abdomen was healthy. So were the lungs.

"On opening the pericardium it was found to contain between four and five ounces of turbid serous fluid, and flakes of coagulable lymph floating in it. The internal surface of the membrane, both where it constituted the exterior bag, and the reflected layer upon the heart, was covered in various situations with a thin layer of lymph exhibiting a reticulated appearance. The size of the heart was natural in relation to the age of the patient. Upon cutting through its parietes the fibres were exceedingly dark colored, almost of a black appearance. This evidently depended on the nutrient vessels being loaded with venous blood. The fibres were also very soft and loose in their texture, being easily separable, and with facility compressed between the fingers. Upon looking closely to the cut surface exposed in the section of either ventricle, numerous small collections of dark-colored pus were visible in distinct situations among the muscular fasciculi. Some of these depositions were situated deeply, near to the cavity of the ventricle, while others were more superficial, and had elevated the reflected pericardium from the heart. The muscular fibres of the auricles were also softened in their texture, and loaded with blood, but without any collections of pus between them. All the cavities of the heart were loaded with coagulated blood. The internal lining, valves, and every other part of the organ exhibited nothing worthy of remark, except the state of general turgescence in the capillary vessels, which had also extended to the lower part of the trachea, bronchi, etc."

This case serves well to show that we may have inflammation of the muscles of the heart, sufficiently severe to cause death in a few days, without a single symptom to call special attention to that organ.

It also indicates, though in an unusually marked manner, the character of the general symptoms on which we have to rely for a diagnosis. There are absolutely no physical signs by which the existence of myocarditis can be determined. There may be indications of cardiac weakness, the impulse may be diffuse or the apex-beat imperceptible, and the first sound muffled or indistinct—but this is not enough for a diagnosis. It is to the general symptoms that we have to trust; and these are essentially the indications of nervous disturbance—mainly delirium.

Delirium in acute rheumatism is always a symptom of serious import. It is so because of the serious nature of the complications of which it is symptomatic. It occurs (1) in hyperpyrexia; (2) in myocarditis; (3) in pericarditis, and (4) in pneumonia, arising in the course of acute rheumatism.

In hyperpyrexia there is the thermometer to guide and give precision to our diagnosis. In pericarditis and in pneumonia equal precision is obtained from a physical examination of the heart and lung. But in myocarditis we have no such aid, and we have to trust to the general symptoms only.

It may be stated generally that delirium arising in a case of acute rheumatism complicated neither with pericarditis nor pneumonia, and in which the temperature is not over 105°, is symptomatic of myocarditis. The delirium may be acute, generally it is low and muttering. With it there are sometimes noted muscular tremors which may give to the patient somewhat the appearance of one suffering from delirium tremens.

Case XIII.—A man, aged 25, of irregular rather than of dissipated habits, had an ordinary attack of acute rheumatism with the characteristic joint affection and acid sweats of the disease. The temperature ranged from 102° to 103° F. He was treated with salicylate of soda. His joint pains decreased, but his general condition did not improve. On the eighth day of his illness he was very prostrate, there was some tenderness on pressure over both wrists, the left knee, and right shoulder, but the joint indications were not marked; there was very little swelling and pain was not complained of except on pressure or movement; temperature was 103.8°, tongue furred, pulse 120, feeble; the heart's sounds were muffled and indistinct, but no bruit could be detected; the area of cardiac dulness was normal; the impulse was scarcely perceptible; the patient was prostrate and sunk in bed; there was wandering at night and occasionally during the day. Patient was freely stimulated, but gradually sank and died. On post-mortem examination all the organs were healthy except the heart. The pericardium contained about an ounce of dark-colored serous fluid; around the roots of the great vessels at the base there was a slight deposit of recently effused lymph, but the general surface of the pericardium was smooth and glistening. The muscular substance of the heart was dark in color and had the appearance of being gorged with blood; it was soft in consistence, and could be broken down by firm pressure between the finger and thumb; under the microscope the individual fibres were seen to have lost much of their normal striated appearance and to be granular in aspect. There was slight roughening of the auricular surface of the mitral valve; but no other appearance of endocardial mischief.

The general aspect of the patient in this case was not unlike that noted in some cases of hyperpyrexia, and had there been a high enough temperature one would not have hesitated to call it so. Post-mortem examination verified the accuracy of the diagnosis formed during life, that the alarming symptoms were due to inflammation of the muscular substance of the heart.

Case XIV.—A man, aged 40, had an ordinary attack of acute rheumatism with inflamed and swollen joints, sweats, and a temperature varying from 101 to 102.4°. He was treated by alkalies and salicylate of soda. Though his pains were less and the temperature fell a little he did not make satisfactory progress. On the seventh day of his illness the temperature was 101°, the pulse was 108, feeble

and compressible; the skin was moist, the perspiration acid; the tongue moist and furred; there was pain and swelling in both ankles, right knee, and both wrists. The patient was depressed and sunk in bed; the hands were tremulous; he wandered at night and occasionally during the day; the bowels were moved by medicine. The area of cardiac dulness was normal—there was no bruit, but the sounds were indistinct and muffled, and the apex-beat could not be felt. The diagnosis was myocarditis—inflammation of the muscular substance of the heart. He was ordered to have every two hours four ounces of milk or strong beef-tea with half an ounce of brandy; all movement was forbidden; as medicine fifteen grains of salicin were given every two hours a quarter of an hour before food. He gradually improved, the muttering delirium ceased, the tongue cleaned, he was less sunk in bed and got some hours of quiet sleep, and the joint pains disappeared. On the nineteenth day there was heard for the first time a distinct pericardial to-and-fro rub audible only at the base of the heart. This persisted for two days and then disappeared. Cardiac dulness remained normal and there was no evidence of fluid effusion into the sac of the pericardium. The patient picked up slowly, but ultimately got well. A year after his illness I examined the heart and found nothing amiss in it.

By various observers attention has been directed to the occasional occurrence of sudden death in acute rheumatism. It is probable that the explanation of this result is to be found in inflammatory softening of the ventricular walls. It certainly was so in the following case:

Case XV.—A girl, aged 20, who had previously enjoyed good health, suffered from an attack of acute rheumatism in March, 1872. The attack was an ordinary one of medium severity, presenting no unusual feature, but complicated by a slight attack of endocarditis which gave rise to no subjective symptom, and the only sign of whose existence was a soft and short systolic blow at the apex. She was treated with acetate of potassium, ten grains every three hours (the case occurred before the days of the salicyl treatment). The endocardial blow persisted, but the rheumatic symptoms had diminished in severity by the end of the second week. On the seventeenth day of her illness she got up of her own accord. Her sister, who was in the room, stated that her feet had scarcely touched the floor, when she fell back on her bed, and lay there motionless. She never moved or gave any sign of life. I saw her twenty minutes later, quite dead. A few minutes before making the effort she expressed herself as feeling very well, and free from pain.

On post-mortem examination the mitral valve was found to be somewhat thickened, and on its auricular surface was a line of lymphy deposit. The heart's substance, especially that of the left ventricular walls, was rather dark in color, and softer than natural. On firm pressure it broke down under the finger. On microscopic examination the normal striæ were wanting in distinctness, and the fibres had a granular aspect. There was a little effusion into the pericardium. There was no ulceration of the endocardial surface, no ap-

pearance of embolism; nothing to explain the fatal result, except the altered condition of the ventricular walls. The cranial and abdominal contents were normal.

Case XVI.—A man, aged 33, who had had several attacks of acute or subacute rheumatism, had what he regarded as one of his ordinary attacks, which he tried to manage for himself with his usual mixture of salicylate of soda, without going to bed. Getting worse, I was asked to see him. I could not go, and asked a *confrère* to do so. He reported to me that the man had subacute rheumatism with a temperature of 101°, but that he had symptoms of delirium tremens as well, though he did not think he had been taking much stimulant. I knew that he was a man of steady habits, and thought it likely that the tremors and delirium were symptomatic of myocarditis, and arranged to see him the following day; but in the mean time while undressing to get into bed he suddenly died. No post-mortem could be got. I had seen the man some months before and examined the heart, which was then quite healthy. There was, therefore, no old-standing heart trouble to account for the death. But there were during life the nervous symptoms which accompany myocarditis, and there can be little doubt that this was the cause of death. Indeed symptoms resembling those of delirium tremens, coming on in the course of acute or subacute rheumatism in a man of steady habits and in whom there is no great rise of temperature, are almost certainly due to myocarditis.

The post-mortem appearances presented in cases of myocarditis, like the symptoms during life, are not very obvious, though quite distinct when carefully looked for. They consist chiefly in loss of consistence in the ventricular walls, for the disease is generally limited to the left ventricle. The muscular substance is darker in color than natural, it has lost its naturally firm consistence, and may be so soft as to break down on being pressed between the finger and thumb.

On microscopic examination the individual fibres are seen to have lost more or less completely their normal striated appearance and to be granular in aspect. The inflammation may even go on to suppuration, as in Mr. Stanley's case already quoted. But that is rare.

The treatment of myocarditis essentially consists in keeping the heart agoing till the inflammation is over and the weakened muscular fibres regain their normal condition. Absolute quiet and rest must be insisted on; good nourishment and a liberal allowance of stimulants are important. Opium may be of service by relieving pain, allaying restlessness, and storing nerve power. At the same time the rheumatism to which the myocarditis is attributable is not to be lost sight of. The undoubted tendency of the salicylates to disturb the nerve centres and enfeeble the cardiac action in a certain number of cases is a reason why they should not be given; but salicin, which has no such untoward effect, should be given in a sufficient dose to counter-

act the rheumatic process—fifteen to twenty grains every two or three hours.

When the acute symptoms are subdued and the immediate danger of heart failure is over, a distinctly tonic treatment is called for.

The Action of the Salicyl Compounds in the Heart Complications of Rheumatism.

In its general pathology, rheumatism of the heart is identical with rheumatism of the joints. The poison is the same; the textures which chiefly suffer are the same; and there is no difference in the mode in which the poison acts. The morbid process is, therefore, fundamentally the same in both.

Such being the case, it is natural to suppose that both should yield to the same treatment, and that the beneficial results which follow the administration of the salicyl compounds in rheumatic inflammation of the joints should equally follow their administration in rheumatic inflammation of the heart. And such no doubt would be the case, if the heart were in all respects similarly situated to a joint. But it is far from being so; for though in their general pathology the two are identical, there exist between them several important differences, the recognition of which is essential to the formation of a just estimate of the respective value of the salicyl compounds in the treatment of each.

In both heart and joints it is the fibrous textures which suffer first and chiefly. In both heart and joints these textures have the same duties to perform—they regulate movement and resist strain. The chief difference to be noted between them is in their relative functional activity. A joint acts only occasionally, never for more than a few hours in succession, and gets complete rest for many hours every day. The heart gets no rest, but beats on by day and by night without cessation or repose. This physiological difference exercises a vast and important influence in disease, and especially in such acute inflammation as that which now engages our attention.

To an inflamed organ rest is of the utmost importance. If a joint is inflamed it becomes painful; motion increases the pain; instinctively we give it rest, and its function is in abeyance till the inflammation is at an end. If a man suffering from rheumatic inflammation of the knees and ankles were to persist in going about as usual (supposing such a thing to be possible), he would thereby prevent recovery. The salicyl compounds might be given so as to destroy the rheumatic poison, but the continued exercise of the inflamed textures would keep up the inflammation, independently of the cause

which originally set it agoing, and they would probably not recover till they got rest.

When the heart is inflamed it gets no rest; no matter what the consequences to itself, its work has to be done; and done it is, so long as life lasts. The fever of the accompanying joint affection, as well as the inflammation of its own textures, causes increased excitability and increased frequency of action, so that instead of rest there is greater activity—instead of its function being in abeyance it is exalted. This it is which makes the chief difference between the results of rheumatic inflammation of the heart and similar inflammation of a joint; and this it is which makes the heart trouble so much less amenable to treatment.

In considering the question of their respective amenability to treatment it is essential that this should be borne in mind, and that the results of the inflammatory process should be distinguished from those directly due to the action of the rheumatic poison. The destruction of the rheumatic poison must put a stop to its direct action on the heart as well as the joints. But to do this is quite a different thing from removing the morbid products resulting from that action. It is a step, and a very important one, toward that end; but something more is requisite to its complete attainment. For this the inflamed textures should have rest. In the joints this is easily got; in the heart it is unattainable. The inflamed valves continue to be strained, their roughened surfaces continue to rub, the friction keeps up the irritation, and restoration to the normal is thus rendered very difficult.

If the heart suffer, it does so for the same reason that a given joint suffers—because its textures are a nidus for the propagation and action of the rheumatic poison. If the heart contain this second factor it does so naturally and before the rheumatic poison gains entrance to the system. It is, therefore, in danger from the very first; and theoretically there is no reason why it should not give evidence of disturbance at as early a period as the joints. Practically, there is very good reason why it should not do so.

The symptoms of rheumatic inflammation of the fibrous textures of a joint are prominent from the commencement of the attack; those of rheumatic inflammation of the fibrous textures of the heart are more tardily developed, and are not apparent till these textures have suffered for some time.

In both joint and heart the fibrous tissue is the part which suffers first. In the joint the inflammation extends from the fibrous textures to the synovial membrane; in the heart from the fibrous rings and valves to the endocardial lining. Before the synovial membrane be-

comes affected, there is already pain, tenderness, and all the evidence of inflammation of the fibrous textures. But until the mischief has extended to the endocardium, there is no evidence of its existence and no possibility of diagnosing inflammation of the fibrous textures of the heart; for such inflammation gives rise to no symptoms or signs until the membrane is roughened.

The signs of endocarditis (to which for the present we shall confine our attention) are those of roughening of the endocardial surface of a valve; but such roughening is not produced by the direct action of the rheumatic poison on the lining membrane; it results from friction of the valvular surfaces consequent on inflammatory thickening of the subjacent fibrous textures.

It follows from this that there is a stage of the endocarditis which precedes the roughening of the endocardial surface, and precedes, therefore, the earliest evidence of the heart affection. In other words, rheumatic endocarditis cannot be diagnosed till the ailment has existed for one or more days. An endocarditis whose physical signs first become apparent on a Wednesday has almost certainly begun on Monday or Tuesday, if not sooner. If the rheumatic poison affect a joint and the heart simultaneously, pain, the earliest evidence of joint inflammation, will precede, possibly by some days, the endocardial blow which is the earliest indication of the heart being affected. The rapidity of development of the endocardial murmur will vary with the acuteness of the attack; but in any case its comparatively late development will make the cardiac inflammation appear secondary to that of the joints, though the two may in reality have originated simultaneously.

The point is that while rheumatic arthritis is diagnosed as soon as it occurs, rheumatic endocarditis cannot be diagnosed in its earlier stages, for it gives rise to no symptoms and no physical signs before the valvular surface is roughened.

Keeping before us these special peculiarities of rheumatic endocarditis, we are in a position to take up the important question of the action of the salicyl compounds in such inflammation.

The question has naturally two aspects—a prophylactic and a curative:

1. Do the salicyl compounds tend to prevent heart complications in acute rheumatism?

2. Do they have a curative action on these after they have occurred?

We shall first deal with the prophylactic aspect of the question.

That a remedy which rapidly cures acute rheumatic inflammation of the joints should tend to ward off, if not prevent, the heart com-

plications which so frequently accompany such inflammation, s a reasonable supposition. And sanguine hopes were at one time entertained that such an action the salicyl compounds would have. These hopes have not been realized. Numerous cases have been recorded in which heart complications have appeared in the course of acute rheumatism, after the salicyl treatment had been commenced.

How is this to be reconciled with the views advanced, first, as to the pathology of rheumatic inflammation of the heart; and, second, as to the mode of action of the salicyl compounds? If it be the case that rheumatic inflammation of the heart is produced in the same way as rheumatic inflammation of a joint, and if it be the case that the salicyl compounds rapidly cure the joint inflammation by destroying the rheumatic poison, should not these compounds, in virtue of that action, ward off and arrest the course of heart inflammation? Theoretically, yes; practically, no. And "no" for the following reasons:

The earliest evidence of the existence of endocarditis is the development of an endocardial murmur. But the roughening of the valvular surface which gives rise to this murmur marks a comparatively late stage of the endocarditis; before it can occur there must be:

1. The reproduction of the rheumatic poison in the fibrous structure of the valve;
2. Proliferation of the cellular elements of this structure.
3. Swelling and thickening of this fibrous structure, and consequent bulging of the endocardium over the seat of the swelling;
4. Rubbing of one swollen segment against another;
5. Roughening of the endocardial surface as a result of this friction.

It is not till all this has taken place that a murmur is developed or a diagnosis made; so that the rheumatic poison has been exercising its action on the heart for one or two days before there are any signs of its doing so. If the salicyl compounds be given to a man just after the fibrous textures of the heart have begun to suffer, they are not given in time to stop the action of the rheumatic poison on them, or to prevent proliferation of the cellular elements; they are not given in time, therefore, to prevent swelling of the valves and rubbing of their segments, and, consequently, not in time to prevent those changes on the endocardial surface to which that rubbing gives rise.

The development of an endocardial murmur after the commencement of salicyl treatment seems to indicate that this treatment possesses no power to prevent cardiac complications. More careful inquiry shows this conclusion to be hasty, and probably erroneous; for not only is some time required for the development of an endocardial

blow, but, as we know from what is observed in rheumatic inflammation of the joints, it takes another day to get the full action of the salicyl compounds. A man may begin to take these compounds on Monday, and on that day the heart's sounds may be quite normal. On Tuesday his joint inflammation may be much better; but there may be an endocardial blow. From the coincident decline of the arthritic and development of the cardiac symptoms the inference might naturally be drawn, and has in several cases been drawn, that the salicyl compounds have no power to prevent cardiac complications in rheumatism. But a careful examination of all the circumstances of the case would lead to a more cautious, if not different, conclusion. Any prophylactic property possessed by the salicyl compounds in rheumatic inflammation of the heart must be due to their destructive action on the rheumatic poison. But this saving action cannot be got unless they are given before the poison has begun to act on the heart; for with the commencement of morbid change in that organ terminates the period of possible prophylaxis.

But even if the start were fair and equal—even if the salicyl treatment commenced at the same moment that the rheumatic poison began to act on the fibrous textures of the heart—the morbid process would still have the advantage, for probably twenty-four hours would elapse before there could be introduced into the system the quantity of the salicyl compounds requisite to the destruction of the poison.

During these twenty-four hours the rheumatic poison would have time and opportunity to cause such change in the fibrous textures as would lead to thickening of the valves, to consequent friction of their segments, and to the development of the signs of endocarditis; while the continued activity of the inflamed tissues would prevent the decline of the inflammation which might otherwise be expected to follow the destruction of the rheumatic poison.

It is impossible to state with exactitude either, on the one hand, the time which, in a given case, must elapse between the commencement of cardiac inflammation and the development of an endocardial blow; or, on the other, the quantity of the salicyl compounds requisite to destroy the rheumatic poison. The former must vary with the acuteness of the attack, the latter with the amount of poison in the system at the commencement of treatment, and with the stage of the disease at which treatment commences. In no given case can we positively assert that the absence of heart complications is due to the preventive action of the salicyl compounds. All that we can do is to satisfy ourselves, first, as to the mode in which the heart complications are brought about; and, second, as to the manner in which the

salicyl compounds act. Having done this, we are in a position to judge as to whether or not they are likely to possess any prophylactic properties.

It has been abundantly proved that the salicyl compounds do possess the power of arresting and cutting short the course of rheumatic fever. This means that they possess the power not only to allay the inflammation which already exists, but also to prevent that which would certainly arise, either in those joints which have already been affected, or in others if the attack were prolonged. If we admit their power to prevent rheumatic inflammation of the joints, we must also admit their power to prevent similar inflammation of the heart. If the view which has been advanced as to their mode of action be correct, they cannot fail to prevent cardiac complications, if only they are given in sufficient quantity to destroy the rheumatic poison before this has begun to affect the heart. The chief obstacle to their doing so is the early stage at which the heart is apt to suffer. It is only in a minority of cases that time and opportunity are given to get the full action of the salicyl compounds before the heart is affected. This is specially the case in hospital practice, in which the patients seldom come under notice before the disease has existed for the best part of a week.

The very acute cases which come under observation during the first two or three days of the illness are also the ones in which the heart is apt to be affected from the commencement. In such cases the joint and heart affection are often contemporaneous, though, for reasons already given, the symptoms of the heart trouble are more slowly developed.

In subacute cases the symptoms are developed less rapidly, and the evidence of the heart affection is more likely to be delayed a few days; but so also is the period at which treatment commences, for such cases are generally ailing for at least three or four days before they come under notice. In acute cases the heart affection is developed so soon and so quickly, that there is not much time to get the prophylactic action of the salicyl compounds. Subacute cases come under notice at so comparatively late a period that there is not much opportunity to do so. So that whatever prophylactic properties we may accord to the salicyl compounds on theoretic grounds, there remains the difficulty that in actual practice this result is not readily got. We know that it may be got; but in no given case can we be sure of having got it. With such a possibility before us, however, and with such a tremendous issue at stake, it is impossible to exaggerate the importance of the early and free administration of the salicyl compounds in all cases of acute and subacute rheumatism;

for we never know when we may be dealing with a case in which prophylaxis is attainable. The bare possibility of such a result is worth striving for. But promptitude and decision are requisite to success. Thirty grains should be given every hour till the temperature is normal and pain gone. A delay of a few hours in commencing treatment, or the administration of the drug in insufficient dose, may make all the difference between perfect recovery and recovery with a damaged heart—a calamity which in some cases is scarcely preferable to death, so hard may be the conditions under which life is carried on.

Do the salicyl compounds have a curative action in rheumatic inflammation of the heart?

Regarding such inflammation as identical in nature and pathology with rheumatic inflammation of the joints, and recognizing the distinctly curative effects of the salicyl compounds in this, it might, not without reason, be expected that they should have the same action in rheumatic inflammation about the heart. Experience, however, has shown that such is not the case, and that under the salicyl treatment, as under all other, rheumatic endocarditis (to which we shall still confine our attention) is apt to leave some trace behind.

Attention has already been drawn to one obstacle which intervenes to make the treatment and cure of inflammation of the heart specially difficult—the impossibility of giving rest to the inflamed textures. This is an obstacle which no treatment can overcome. It is an important factor in keeping up the mischief originated by the rheumatic poison, and affords an adequate explanation of the fact that the treatment which rapidly allays acute rheumatic inflammation of a joint may fail to have a like action in similar inflammation of the heart. In both rest is essential to quick recovery. In the one it is easily got; in the other it is unattainable.

But it is not enough to explain why the ailment should be so little amenable to treatment during its acute stage. We have also to explain why the endocardial mischief is so apt to be lasting.

Pericarditis may be perfectly recovered from, the effused products may be absorbed, and the membrane restored to its natural state. So too may myocarditis. But in endocarditis the signs are apt to persist after all inflammatory mischief has ceased. It is a pathological fact that when once a certain amount of change has taken place on the endocardial surface the damage is apt to be permanent. The endocardium is the only structure habitually affected by the rheumatic poison of which this can be said; it is also the only structure in the heart which has no analogue, anatomical or physiological, in the joints. The fibrous and muscular textures of the heart and joints

have a like structure and function. So have the pericardial and synovial membranes. The endocardium alone is unrepresented in the locomotor apparatus. It stands alone, too, in its pathology. Its scanty vascularity and low vital activity make it insusceptible to acute general inflammation. Such inflammation is, therefore, unknown in connection with it. The same circumstances intervene to prevent the absorption of products effused on its valvular portion during an attack of rheumatic endocarditis. To the absorption of such products a certain degree of vascularity is necessary; such vascularity does not exist in the endocardium.

It may, indeed, be said that a degree of vascularity which suffices for the effusion of lymph, should suffice also for its absorption. But the deposit on the valves is not all effused. Great part of it is deposited directly from the blood, on the roughened surface; and even the primary roughening results from irritation caused, not directly by the rheumatic poison, but by friction of the valvular surfaces—a mechanical force which, in the case of the endocardium, cannot be equalled or counterbalanced by any agency which stimulates absorption.

It is evident that the condition is one on which drugs can have no direct action; and thus is explained the inability of the salicyl compounds to repair the damage done during an attack of rheumatic endocarditis.

The direct cause of all the objective, and most of the subjective, symptoms of endocarditis is not the rheumatic poison which causes the inflammation—it is not even the inflammation itself—it is the physical change caused by the rubbing against each other of the swollen valves. The lymph deposited during rheumatic inflammation of the heart differs in no respect from that thrown out during non-rheumatic inflammation. No one would expect the salicyl compounds to remove the latter. It would be as unreasonable to expect them to remove the former. These drugs are not deobstruent, they are anti-rheumatic. They cure rheumatic fever; but they do not stimulate absorbents, or remove effused products.

The fact that the salicyl compounds are powerless to remove cardiac damage is an urgent reason for getting the system under their influence, before the heart becomes involved.

But though they fail to effect a cure, it cannot be said that these compounds have no beneficial effect in cardiac inflammation. For if they have a destructive action on the rheumatic poison they cannot fail to be of some benefit. If they destroy this poison, they must by so doing curtail the duration and limit the extent of its action on the heart, and so mitigate the severity of the cardiac mischief.

But this is not the only way in which they tend to do good. Under their influence the joint inflammation subsides, and the febrile disturbance is allayed. This result is of course accompanied by diminished frequency of the heart's action as well as fall of temperature. The cardiac pulsations may fall from 112 to 72—a fall of 40 a minute, 2,400 an hour, or 57,600 a day. This diminished frequency of the heart's action implies decreased functional activity of the inflamed textures; and this quieting of the heart's action is the one condition which is most desired and most difficult to attain, in the treatment of rheumatic inflammation of the heart. Were the rheumatic process not thus cut short the rheumatic poison would continue to act for some weeks; the heart would continue to beat at the rate of 112 per minute, if not more; the inflamed valves would every day be subjected to the strain involved in their action 57,600 times more frequently—an enormous difference which could not fail to tell injuriously.

It is evident that independently of the good which must directly result to the heart from the destruction of the rheumatic poison and the consequent cessation of its action on the cardiac structures, benefit must accrue to that organ from the diminished frequency of its own action, consequent on the arrest of the joint inflammation and accompanying fever.

The general conclusion to which we are led is, that the early and free administration of the salicyl compounds holds out the best chance both of saving the heart from the action of the rheumatic poison and of mitigating the severity of that action when it is too late to prevent it; but that these compounds are powerless to remove effused products, after the heart mischief is established.

The general treatment applicable to rheumatic inflammation of the heart is thus the same as that which is applicable to similar inflammation of the joints. The existence of heart complication in a case of acute rheumatism is not only not a reason for omitting the salicyl compounds, but is an additional one for giving them freely, and in large dose.

In the great majority of cases no other treatment is required. But every now and then a case occurs in which considerable benefit is got from the adoption of local measures. In pericarditis especially, local treatment is sometimes of much service. In the early stage of a severe attack, when pain is a prominent symptom, when the heart's action is disturbed and tumultuous, and when there is evidence of serious interference with the circulation, much good may be got by abstracting a few ounces of blood. This may be done by opening a vein, or by the application of leeches or cupping-glasses

over the region of the heart. If the symptoms are urgent, venesection affords the most speedy relief; but to do good it must be had recourse to at an early stage. The cases are few, however, in which the desired effect may not be got from leeches.

In entertaining the question of bleeding, local or general, it must be borne in mind that the acute stage, when got over, is followed by one in which there is apt to be considerable debility. If bleeding be had recourse to unnecessarily or too freely, this stage will be rendered more marked and prolonged. The mere existence of acute pericarditis is not a reason for taking blood; such a measure is to be regarded only as the best means of allaying the urgent symptoms of the first stage of a very acute attack.

Cold, as got by the application of an ice-bag over the region of the heart, may be of benefit at this stage. It is to be prescribed only during the acute stage. In milder cases warm poultices often give relief.

After the acute stage has been subdued, there is generally, especially in severe cases which have required active treatment, some effusion of fluid into the pericardium. In most cases this disappears as convalescence advances and strength returns. But occasionally it is necessary to adopt measures for its removal.

Blisters repeatedly applied over the heart, and the internal administration of deobstruents, such as iodide of potassium, are the remedies usually recommended. Blisters are certainly of use; but the debilitated condition of the patient and the weakened state of the cardiac muscles, which suffer more or less in acute cases, indicate the use of good food and tonics.

If these measures fail, and especially if the quantity of fluid be so great as to cause serious inconvenience, it may be necessary to have recourse to tapping. The trocar of an aspirator may be introduced into the distended sac without difficulty. The best point for its insertion is the fifth intercostal space, to the left of the sternum, care being taken to avoid the line of the internal mammary artery. Whether or not the operation may be ultimately successful, it always affords relief for the time. But the operation is one which is rarely called for.

In endocarditis it is very questionable if local measures ever do good. If the case is very acute, and accompanied by evidence of distress, a few leeches may be applied. But all depletory measures should be used with extreme caution. So, too, should they be in myocarditis.

There is no especial treatment applicable to myocarditis; it is essentially symptomatic. But, as a rule, the treatment of the acute

stage is the same as that of endocarditis. When that stage passes off, the administration of tonics is called for. In acute cases in which there is serious impairment of the vigor of the muscular walls of the heart, stimulants should be given freely.

Attention has already been drawn to the change in the cardiac walls, induced by inflammation. They become abnormally soft and weak. It is at all times of importance that the occurrence of such a change should be recognized. It is specially so in connection with the salicyl treatment; for one of the drawbacks to the use of salicylic acid is its depressing action on the heart, evidenced by feebleness and generally increased rapidity of its action.

In the treatment of the heart complications of acute rheumatism it is of importance that this action of salicylic acid should be borne in mind. If there is any reason to suspect the existence of inflammatory softening of the walls of the heart, salicylic acid, if given at all, should have its action on the heart watched very narrowly. If there is any evidence of the existence of myocarditis, or of feeble cardiac action, it should not be given at all; for the addition to the already existing enfeeblement of such depression as salicylic acid may cause might add seriously to the patient's danger. It is not in every case that salicylic acid has an enfeebling action on the heart, but one never knows when such a case may occur. To give a remedy which may have such an action, in an ailment in which cardiac enfeeblement is the special danger with which we have to deal, is a practice which one cannot commend, for it cannot fail at times to produce injurious results. Fortunately it is a practice which is never called for even in the interests of the joints; for we have in salicin a remedy which, as an anti-rheumatic, is as potent as salicylic acid; and which possesses over that acid the enormous advantage of having no depressing action on the heart. In all cases of recent inflammation of the heart, the muscular substance is liable to be affected. In all cases in which it is affected, there is produced a soft and enfeebled condition of the ventricular walls. In all such cases the administration of salicylic acid is attended with appreciable risk.

Rest, quiet, good food, tonics, and stimulants in moderate quantity, are the remedial agencies to which we must trust in the treatment of this softened condition of the heart's walls.

The ailment is one which nearly always occurs in young people; at an age, that is, at which the system possesses great recuperative powers. If not fatal in the acute stage, recovery is generally perfect. Attention has already been drawn to the fact that it may cause sudden death. The risk of such an accident would be increased by the de-

pressing action of salicylic acid given either plain or as salicylate of soda. No such risk attends the use of salicin.

The injurious effects of the ordinary commercial salicylic acid (made from carbolic acid) are said to be due to impurities, and Professor Charteris of Glasgow has indicated creasotic acid as the special impurity. The natural salicylic acid, made from salicin or from oil of wintergreen, is said to be free from depressing effect. Even if that be so it has no advantage over salicin, the most easily obtained of all the natural salicyl compounds, and one which we know to be quite safe.

Cerebral Rheumatism.

Head symptoms occurring in the course of acute rheumatism constitute the most formidable complication of that disease. There is indeed no malady in which delirium is of such grave import. It is so because of the grave nature of the complications of which it is symptomatic. It occurs under three conditions:

1. In connection with inflammation of the membranes of the brain;
2. In connection with inflammation of the heart, or of its investing membrane;
3. In connection with hyperpyrexia.

Rheumatic Meningitis.

There are recorded a few cases of acute rheumatism in which the occurrence of marked head symptoms during life, and the presence of lymph, and even pus, on the surface of the brain after death, show that meningeal inflammation may occur in the course of that disease. But meningitis occurring in the course of acute rheumatism is not necessarily of rheumatic origin. The extreme rarity of such cases, indeed, suggests a doubt whether, in the few cases in which it did occur, the meningeal mischief was not an accidental complication, due to the action of some other agency than the rheumatic poison. Certain it is that the very small proportion of cases in which such a complication occurs detracts from the interest and importance which would otherwise attach to it. Of all possible causes of head symptoms occurring in the course of acute rheumatism, inflammation of the membranes of the brain is the least likely to be the one with which, in a given case, we have to deal.

The symptoms of such inflammation would not differ from those of similar inflammation occurring independently of rheumatism. Its treatment, too, would be the same, except that appropriate anti-rheu-

matic remedies would be conjoined with the measures specially suited to the local head affection.

The Nervous Symptoms of Carditis.

To the occurrence of head symptoms in connection with inflammation of the heart and its membranes, attention has already been directed; and two cases have been given in which all the symptoms during life pointed to inflammatory mischief within the cranium, but in which after death there was found nothing abnormal within the head, but only the indications of inflammation of the heart and its investing membrane.

Since these cases were recorded, much attention has been given to this subject, and the observations of Bouillaud, Macleod, Hawkins, Bright, Burrows, Latham, Fuller, Watson, and others, have demonstrated that inflammation of the heart and pericardium is a frequent cause of head symptoms in acute rheumatism. It is chiefly in connection with pericarditis that they have been noted; this is no doubt because it is more frequent and more readily diagnosed than myocarditis. As already remarked, it is probable that the head symptoms attributed to the pericarditis are in many cases indicative of a coincident myocarditis.

In studying the pathology and mode of production of the symptoms three possible causes have to be considered:

1. The morbid condition of the blood;
2. The cardiac inflammation;
3. The nervous constitution of the sufferer.

1. *A morbid condition of the blood* was the explanation on which our fathers, with the views which they held regarding the pathogenesis of acute rheumatism, naturally fell back. "A distempered condition of the blood I conceive to be the true proximate cause of the sensorial disturbance occasionally observed in the course of acute rheumatism" (Fuller).

"Those remarkable cerebral affections—the wild delirium and violent mania—which not unfrequently occur in the course of rheumatic fever, or follow in its train, and which have usually manifested themselves along with the cardiac complications, causing doubt and perplexity in the mind of the physician as to the real organ affected, and the true nature of the disease, are to be explained by the morbid condition of the blood which is admitted to exist in the rheumatic constitution" (Begbie).

But this morbid condition of the blood exists in every case of rheumatic fever. If it sufficed for the production of nervous symp-

toms, such symptoms would be the rule and not the exception, and delirium would be as common in rheumatic fever as it is in typhus. Such an explanation, too, rather leaves out of account the heart trouble in connection with which these symptoms are noted.

2. *The Cardiac Inflammation.*—Recognizing the insufficiency of this hypothesis, Sir Thomas Watson thought these symptoms might be due to disturbance of the cerebral circulation, resulting from embarrassment of the heart's action. The objection to this view is that the cases in which nervous symptoms are most marked are not, as a rule, those in which evidence of cardiac embarrassment occurs, but, on the contrary, those in which there are no subjective symptoms of heart disturbance, and nothing to direct special attention to that organ. The heart's action may be more embarrassed when the inflammation affects the membranes, than when it is confined to the muscular substance.

But inflammation of the muscular substance causes more marked nervous symptoms. Cardiac embarrassment causes its own special symptoms, but disturbance of the nervous centres is not one of these. Such symptoms are more noted in cases of myocarditis in which there are no cardiac symptoms to attract attention—Corvisart's latent cases.

3. *The Nervous Constitution of the Patient.*—It is not unlikely that individual susceptibility may in some cases have something to do with their production. In all acute febrile ailments nervous symptoms are apt to occur. They are especially apt to do so in persons of susceptible and delicate nervous organizations. In his remarks on his case of pericarditis with delirium already quoted Andral says: "Qu'en raison des susceptibilités individuelles, il n'est point d'organe dont la lésion ne puisse déterminer les symptômes nerveux les plus variés, de manière à produire sympathiquement les différens états morbides dont on place le siége dans les centres nerveux et leurs dépendances."

This individual susceptibility is a factor to be borne in mind in explaining the occurrence of delirium in a given case of pericarditis. But probably a more important factor is the extent to which the muscular substance of the heart is inflamed; for the occurrence of delirium in a case of pericarditis may be regarded as evidence of accompanying myocarditis. This disturbance of nerve centres may be partly due to malnutrition consequent on inefficient cardiac action, but mainly to the disturbance which must result from acute inflammation affecting an organ of such importance as the heart. We have already seen that delirium in some form is the leading symptom in myocarditis.

Rheumatic Hyperpyrexia.

Every now and then a case of acute rheumatism occurs which, after presenting the symptoms of the malady in the ordinary form, suddenly develops alarming nervous symptoms, with a temperature rapidly rising to 107°, 108°, 109°, or even higher, and a tendency to death by coma. Our knowledge of this condition is of recent date, and is one of the results of the more accurate clinical observation to which the use of the thermometer has led. There can be no doubt that many of the cases which our fathers described as cerebral rheumatism were cases of what we would now call hyperpyrexia.

This condition is not peculiar to acute rheumatism. It may arise in the course of any acute febrile ailment, in typhoid fever, measles, pneumonia, pyæmia, etc.; or it may be symptomatic of tumor of the brain, hemorrhage into its substance, or of other injury to nerve centres. We find it in its simplest and plainest form as it presents itself in heat apoplexy. Indeed the symptoms of heat apoplexy, its mode of fatal termination, and the appearances presented after death are exactly those which we find present themselves in hyperpyrexia as it occurs in rheumatic fever, pneumonia, typhoid fever, and other febrile diseases.

Hyperpyrexia is not a disease *per se;* it is a morbid condition which may arise in the course of many ailments. It essentially consists in great rise of temperature, marked nervous symptoms, and a tendency to death by coma. Prominent nervous symptoms are as essential to its existence as the very high temperature to which it owes its name.

It has been supposed by some that the high temperature of the blood causes the disturbance of the nervous centres. The objections to this view are:

First, that it gives no explanation of the occurrence of the high temperature;

Second, that the temperature of hyperpyrexia may occur, as it not unfrequently does in relapsing fever, without causing any disturbance of the nervous system.

There can be no doubt that the process is the reverse of this and that the high temperature is a result of disturbance of nerve centres, ranking with the nervous symptoms, and like them due to the disturbing action of some morbid agency on these centres. It is not simply an exaggeration of the pyrexia of ordinary febrile attacks, but a morbid condition implanted on the pre-existing fever. How is it brought about?

The thermal apparatus of the body consists:

1. Of the tissues in which heat is formed;
2. Of the surface from which heat is eliminated;
3. Of a central controlling power in the nervous centres;
4. Of nerves connecting this with the heat-forming parts of the body;
5. Of nerves connecting it with the heat-eliminating surface.

The harmonious working of these different parts of the thermal apparatus gives rise to the phenomena of thermogenesis, and the general result is a persistent temperature of 98.4°. Interruption of this harmony causes the temperature to rise or fall. Fall of temperature is due either to lessened formation or increased elimination of heat. Rise of temperature is produced either by increased formation or decreased elimination.

Rise of temperature due to direct stimulation of the process by which heat is formed must be brought about by an agency which increases tissue metabolism. Heat is an excretory product, a result of retrograde tissue change, and cannot be produced apart from that change. To say that heat could be directly brought about by stimulation of a heat-producing centre, without increased tissue change, would be to place heat as a product on the same level and in the same category as volition and emotion, which is absurd. Increased heat due to direct stimulation of the heat-producing process must be due to the operation of some agency capable of causing increased activity of tissue metabolism. We can no more have increased formation of heat without increased activity of the processes during which heat is formed, than we can have increased formation of urea or increased formation of carbonic acid without increased activity of the processes during which they are formed. That the continuance of normal tissue metabolism is dependent on influences conveyed to the tissues by the trophic nerves is undoubted. And it is quite conceivable that stimulation applied to the centres whence these trophic nerves proceed might, by causing increased activity of tissue metabolism, give rise to increased production of heat. The experiments of Messrs. Aronsohn and Sachs, in which electrical stimulation of a particular portion of the corpus striatum produced a rise of temperature varying from 2½ to 4½ degrees Fahrenheit, would seem to indicate that fever may be produced by direct stimulation of a certain portion of the nervous centres; and the possibility of such a result must be kept before us in investigating the mode of production of the febrile phenomena of any given disease. But equally must it be borne in mind that such a result could be brought about only by causing increased activity of the metabolic changes by which heat is formed in the tissues. Such a nerve centre can be only one portion of the heat-producing appara-

tus, and it is quite possible that stimulation applied to other parts of this apparatus might cause the temperature to rise without primary stimulation of a nervous centre.

Besides dominating heat-production the nervous centres control heat-inhibition, and by so doing keep the temperature at the normal standard in health, and in disease prevent it from passing due bounds.

Inhibition restrains and regulates functional activity, as the reins restrain and regulate the pace of a spirited horse. Slacken the reins, and he hastens his pace; let them go, and he is off at the gallop. Inhibition is an active, not a passive agency, and is in constant operation. This is well exemplified by the action of the vagus on the heart; stimulation of that nerve slows the heart's action, and if the stimulus be strong enough, may arrest it altogether, the arrest taking place in diastole. But the nervous system which supplies this inhibiting force supplies also another, which, reaching the heart by another channel, has exactly the opposite effect: it stimulates the heart to increased activity. These two forces are in constant operation, and so counterbalance each other that the heart is normally kept beating at the rate of about seventy a minute.

There is no organ whose normal amount of work represents the full measure of its capacity; there is no function whose normal state of activity represents the full possibility of its performance. Each is restrained and kept within physiological bounds by the inhibiting action of the nervous system. Tissue metabolism is no exception to the rule. Normally, tissue formation and tissue disintegration counterbalance each other. But let the reins be slackened, let inhibition of metabolism be impaired, metabolism is necessarily increased and pyrexia results. Let the reins be cast loose, let inhibition be paralyzed, and metabolism, freed from control, is off at the gallop, and hyperpyrexia results. Hyperpyrexia may be defined as paralysis of inhibition of metabolism; paralysis of heat-inhibition being only part of the process.

The clearest and most undoubted cases of rise of temperature resulting from paralysis of heat-inhibition are those in which such rise occurs as a result of a lesion of nerve centres—cerebral tumors, cerebral hemorrhage, or injury to the cervical portion of the cord.

It is impossible to regard the results of such lesions, consisting as they essentially do of pressure upon, or laceration of, a portion of the nervous centres, as other than paralytic in nature. The effect of all such mechanical lesions is not to increase, but to impair or abolish, function—to produce more or less paralysis. The only way in which a destructive and non-inflammatory lesion could cause tempera-

ture to rise is by impairing that function which normally prevents it from rising—in other words, by impairing heat-inhibition. Rise of temperature thus produced will vary according to the extent of the lesion; in slighter injuries there may be no serious damage to the nervous centres, and no greater rise of temperature than is noted in cases of cerebral hemorrhage in which the sanguineous effusion is small and does not open into the ventricles. In more extensive lesions, in which these centres are more seriously damaged (as in severe cases of cerebral hemorrhage in which the effusion is more extensive and tears its way into the ventricles), the temperature rises rapidly and to a much higher point; while the highest temperature of all is noted in cases of crushing of the cord, in which the heat-forming parts of the body may have their connection with the heat-inhibiting centres cut off more completely than is likely to be the case in any intracranial lesion.

Admitting that the nervous system possesses the power to control and limit heat-formation and prevent undue rise of temperature, we have no difficulty in the maladies and injuries to which reference has been made, in attributing the increased body heat to interference with that function. The temperature rises because the reins are slackened. The sequence of events seems to admit of no other explanation. Carrying on this line of argument we cannot fail to see, not only that the rise of temperature thus induced must be directly as the extent to which heat-inhibition is impaired, but that paralysis of this function, by abolishing inhibition and leaving heat-production in uncontrolled possession of the field, must lead to hyperpyrexia. And the more we consider the pathogenesis of febrile heat, the more apparent does it become that impairment of inhibition is a much more likely cause of hyperpyrexia than is direct stimulation of heat-production. Heat-inhibition remaining unimpaired, tissue metabolism could not cause those very high temperatures which characterize some cases of hyperpyrexia. Heat-inhibition being paralyzed, the temperature cannot fail to rise, and to rise rapidly, so long as tissue metabolism and heat-production continue.

All cases of hyperpyrexia we, therefore, regard as of neurotic origin—as due to some cause which exercises a paralyzing influence on the heat-inhibiting function. Pyrexia may result either from increased production or from defective inhibition, but hyperpyrexia is due only to defective inhibition.

In the cases instanced there has been a direct lesion of the nervous centres to explain the paralysis of inhibition. Other cases there are in which hyperpyrexia is as marked, but in which the sequence of events by which it is brought about is not so apparent. Rheumatic

hyperpyrexia is a case in point. Another is heat apoplexy; and it will lead to a clearer understanding of the whole subject if we premise what we have to say regarding rheumatic hyperpyrexia by a brief consideration of the process by which heat apoplexy is brought about.

That continued exposure to a high temperature is likely, in a native of a temperate climate unaccustomed to such exposure, to cause disturbance of the thermal apparatus there can be no doubt.

Heat is an excretory product requiring to be eliminated; its chief seat of formation is the muscles; its main channel of elimination is the skin; a high temperature of the atmosphere necessarily interferes with such elimination, because in such an atmosphere heat cannot readily be thrown off. Heat-elimination being thus checked and heat-production continuing as usual, heat must accumulate in the system, unless some agency steps in either to increase elimination or diminish formation. Under ordinary circumstances nature provides the remedy; for the same atmosphere which makes heat-elimination difficult causes also increased activity of the skin, and so meets the difficulty which itself creates; while the general influence of residence in a hot climate leads to habits of life which diminish tissue metabolism and heat-production; thus the risk of heat-accumulation is diminished at both ends. But circumstances every now and then arise which break through these habits. Such circumstances are those which call for exposure and muscular effort during the heat of the day, as in the case of soldiers on the march. Tissue metabolism and heat-production are stimulated, while the body is exposed to a temperature which makes a corresponding increase in heat elimination difficult. Nature guards against this danger by restraining heat-production. This she does by increased activity of the heat-inhibiting function. The difficulty in the present case is the throwing off of the heat in consequence of the high temperature of the surrounding atmosphere. This difficulty only creates a necessity for more vigorous efforts on the part of the heat-inhibiting centre; this centre continues to work at high pressure, and struggles to keep the temperature down till over-stimulation leads to exhaustion; the struggle is too much for it, its efforts become feebler, it gets more and more unfit to cope with the difficulty, and ultimately, overcome by fatigue, it ceases to act. Thus is removed the last safeguard, heat-production goes on apace, heat rapidly accumulates in the system, and heat apoplexy with its attendant hyperpyrexia results. What takes place in the thermic centre in such circumstances is the counterpart of what takes place in the respiratory centre, when an excess of carbonic acid in the atmosphere, by the ordinary laws of diffusion, prevents the due elimination of that gas from the blood. The first effect of an increase of

carbonic acid in the blood is to stimulate the respiratory centre, and cause increased force and frequency of the respiration. If the amount of gas in the atmosphere be so great as to make its due elimination impossible, that gas accumulates more and more in the blood; the respiratory centre gets fatigued, its efforts become feebler, the respirations become slower, the interval between them longer, and finally they cease. The cause of their cessation is paralysis of the respiratory centre induced by over-stimulation and fatigue; and the cause of this is not the taking in of carbonic acid from without, but the impossibility of eliminating in an atmosphere of that gas the carbonic acid which is formed in the system. So in heat apoplexy, it is not the heat of the surrounding atmosphere which raises the temperature of the body; but in such an atmosphere heat cannot be properly eliminated, it tends to accumulate in the blood, and the only way to prevent disaster is to limit heat-production. With this object the heat-inhibiting centre is stimulated to make unusual efforts. In most cases it succeeds, and the only evidence of the struggle is excessive perspiration and a sense of exhaustion. But the effort may be too much for it, it gets fatigued, its efforts become feebler, production goes on apace, inhibition is in abeyance, the reins are cast loose, and hyperpyrexia results. Thus is explained the hyperpyrexia of heat apoplexy.

Rheumatic hyperpyrexia might be merely an exaggeration of the ordinary pyrexia of rheumatic fever; or it might result from a direct paralyzing action of the rheumatic poison on the heat-inhibiting centre; or it might be produced in the same way as heat apoplexy by over-stimulation and consequent paresis of that centre.

The first hypothesis is scarcely adequate, for were the hyperpyrexia of rheumatic fever merely an exaggeration of the ordinary pyrexia of the disease, cases in which it occurs would be characterized by inordinate severity of the rheumatic symptoms. But such is not the case. In cases which become hyperpyretic the disease up to the onset of the hyperpyrexia may present no unusual features. The temperature, the joint pains, the acid sweats, the heart complications, may all be such as are met with daily in ordinary rheumatic attacks; and there may be nothing in their symptoms to lead the physician to anticipate so alarming a complication.

The hypothesis that it may result from paralysis of the heat-inhibiting centre consequent on the direct toxic action on that centre of the rheumatic poison, or some product of the rheumatic process, is one regarding which no more can be said than that it is possible. Against it may be adduced the argument that were such the mode of production of rheumatic hyperpyrexia, that condition would arise more frequently than it does. The rheumatic poison and the pro-

ducts of the rheumatic process operate in every case, but hyperpyrexia is of rare occurrence. Then again hyperpyrexia occurs in other fevers and other morbid states in which the rheumatic poison does not operate.

The third hypothesis is one for which more may be said, for between heat apoplexy and rheumatic hyperpyrexia there are many points of analogy. The symptoms and clinical features of both are very much alike, and the description of the post-mortem appearances observed in the one serves equally to describe those noted in the other. Treatment, too, is the same in both. The main difference between them is in the circumstances which lead up to their occurrence. With so many points of resemblance between them we cannot but look for a common mode of production, some common pathological bond. The question for consideration is the possibility of the rheumatic process, as it exists in acute rheumatism, producing the same results as we find follow exposure to great heat. The latter acts by over-stimulating, fatiguing, and finally paralyzing the thermic inhibitory centre. The question before us, therefore, narrows itself into a consideration of the point as to whether or not over-stimulation and consequent fatigue of the heat-inhibiting centre is a possible result of the process of acute rheumatism. Wide as is the difference between that process and great heat, and great as seems the improbability of two such different agencies producing the same effect on the system, a careful consideration of the facts, nevertheless, leads to the conclusion that such a result is not impossible. Certain it is that if overstimulation and fatigue of the heat-inhibiting centre, and consequent impairment of heat-inhibition, could be a result of any fever, rheumatic fever is the one in which it would most likely occur, and that for the following reasons:

In all fevers the rise of temperature results from increased tissue metamorphosis. This is the case in rheumatic fever, as it is in typhus, typhoid, and other fevers. But the circumstances under which that increased metabolism takes place in rheumatic fever are altogether peculiar, and the peculiarity of these circumstances it is which leads up to the phenomenon which we are now considering—the greater tendency to the occurrence of hyperpyrexia.

Rheumatism is essentially a disease of the motor apparatus of the body. Part of this motor apparatus—the muscles—is the chief seat of heat production. The more active the metabolism of the muscles the greater the amount of potential energy produced. This potential energy may take the form of work or heat. As a matter of fact, it generally assumes the form of work, for it is when muscles are actively contracting that this potential energy is chiefly

formed. But if the same metabolic changes which take place in a contracting muscle were to take place in that muscle when quiescent, the potential energy would take the form, not of work but of heat. This is what occurs in acute rheumatism. The rheumatic poison causes general febrile disturbance accompanied by inflammation of the muscles and fibrous textures of the large joints. Inflammation of these textures is of course accompanied by increased flow of blood to, and increased metamorphosis in them.

That such increased metabolism as occurs in muscle during work occurs also during the course of rheumatic fever is demonstrated by one of the essential phenomena of that disease, increased formation of lactic acid; and the very large extent to which this acid is formed is indicative of the very large increase of the muscle metabolism to which it owes its formation. Rheumatic fever is the only form of fever in which this occurs, because it is the only one whose poison finds its nidus in muscle. The propagation of this poison in muscle gives rise there to the same increased metabolism which would result from natural stimulation.

Muscle being the chief seat of the formation of heat, and the metabolism of muscle being the chief source of heat, it follows that the disease in which such metabolism is most active is also that in which most heat will be formed. That disease is acute rheumatism. Theoretically, there is thus reason to believe that heat-production is more active in acute rheumatism than in any other disease. There is also practical evidence that such is the case. The natural result of increased formation of heat is its increased elimination. The skin is the channel by which heat is eliminated. Profuse perspiration, the evidence of excessive action of the skin, forms one of the characteristic features of rheumatic fever. Excessive production is thus met by excessive elimination of heat, and no undue rise of temperature occurs.

But another result of such increased activity of the heat-producing process must be stimulation of heat-inhibition. The function of the heat-inhibiting centre is to restrain excessive formation of heat—this excessive formation of heat, though common to all fevers, is most marked in acute rheumatism; that function is, therefore, likely to be called into more active operation in acute rheumatism than in any other disease. It might happen either from want of vigor, or from unusual susceptibility of the nerve centres, aided possibly by more or less failure in the heat-eliminating action of the skin, that heat-production was in excess of heat-elimination. Under such circumstances heat would accumulate in the system. As a result of this the heat-inhibiting centre would be first stimulated to excessive effort, then

fatigued, and finally paralyzed, as in heat apoplexy, and hyperpyrexia would result. That is a sequence of events which might occur in any form of fever or in any ailment, accompanied by increased activity of the heat-producing process. The more active that process the more likely is it to happen. Acute rheumatism, being the ailment in which heat is most abundantly and rapidly formed, is also the one in which inhibition is most likely to be overmatched. Hyperpyrexia is, therefore, more common in it than in any other form of fever.

Though for convenience' sake we refer to paralysis of heat-inhibition as the immediate cause of the very high temperature, it is evident that it is not only heat-inhibition, but inhibition of metabolism in general that is paralyzed. Hyperpyrexia may be defined as paralysis of inhibition of metabolism, heat-inhibition being only part of it. It is not the high temperature that causes the nervous symptoms, but disturbance of an important part of the nervous centres that causes the high temperature. In accordance with this we find that, both in heat apoplexy and in rheumatic hyperpyrexia, the occurrence of the high temperature is generally preceded by headache, giddiness, restlessness, or other indication of disturbance of the nervous centres. All Indian authorities refer to these premonitory indications in the case of heat-apoplexy. In cases of acute rheumatism which become hyperpyretic, there will generally be found evidence of disturbance of the nervous system preceding the hyperpyrexia; and such disturbance should put us on the watch for graver symptoms.

Hyperpyrexia as it occurs in rheumatic fever is not a part of the rheumatic process, but an accidental complication. It is not due, like the joint inflammation and heart complications, to the direct action of the rheumatic poison, and is not to be treated in the same way. The salicyl compounds put a stop to the rheumatic process by destroying the rheumatic poison. They have no controlling influence in rheumatic hyperpyrexia because it is not part of the rheumatic process but an accidental complication of the febrile state which, for the reasons already given, is more common in rheumatic than in other fevers.

Hyperpyrexia essentially consists in paralysis of inhibition of metabolism. Such paralysis may result from either organic lesion or functional disturbance of the nervous centres. The very high temperature to which the condition owes its name is the special indication that the function of heat-inhibition is impaired; just as the very rapid pulse (150 to 160) and the very frequent and hurried respiration indicate that inhibition of the cardiac and respiratory functions is also impaired. When hyperpyrexia is due to organic lesion treatment is

of no avail. When due to functional disorder, as is the case in rheumatic hyperpyrexia, it may be cured. In the treatment of this condition the external application of cold is the remedy on which we chiefly depend. How does the cold act? The opinion generally held is that the cold allays the disturbance by lowering the temperature. But to say that mere lowering of the body heat is sufficient to allay the alarming symptoms, is equivalent to saying that these symptoms are caused by the high temperature, and that we have seen is not the case. In hyperpyrexia the external application of cold not only lowers the temperature but arrests the whole morbid process and cures the patient.

The central thermal apparatus which presides over heat-formation, heat-inhibition, and heat-elimination is necessarily in free communication with the skin, for it is in the skin that sensations of heat and cold are felt, and it is through the skin that heat is eliminated. The superficial nerves which receive the impressions of heat and cold must be connected with the centres in which these sensations are registered, and such centres must be associated with the function of heat-inhibition. It is on the extremities of these nerves that the cold acts, and it is along these nerves that this peripheral excitation is transmitted to the inhibiting centres; the action is essentially a stimulant one; but to stimulate inhibition is the physiological and scientific method of allaying undue functional activity. Just as heat (as in heat apoplexy) paralyzes inhibition and thus causes the temperature rapidly to rise, so cold stimulates inhibition and thus causes this abnormal temperature to fall. Just as it is not the direct heating up of the body by the hot atmosphere that causes the very high temperature of heat apoplexy, so it is not the direct cooling action of cold on the body that cures this condition. The heat acts by impairing, maybe even paralyzing, the function of inhibition; the cold acts by stimulating that function into renewed activity. Its action in this respect may be compared with, and illustrated by, the action of digitalis in some forms of heart disease. When we find the heart acting in an unnecessarily disturbed and excited manner, as it frequently does in mitral disease, we do not combat this condition by efforts to soothe the excito-motor nerve of the heart; no, we rather gain our object indirectly by giving digitalis and stimulating to increased activity the counterbalancing force—the cardiac inhibitory nerve—the vagus. In doing so we adopt a line of treatment which is not only found in practice to be the most successful, but is also the most scientific, and that which is most in accord with the teachings of physiology and the operations of nature.

In hyperpyrexia treatment must be prompt and vigorous. In-

hibition, one of the most important functions of organic life—one which is absolutely essential to the continuance of life—is all but paralyzed. The remedy is the application in full dose of that which stimulates it into increased activity—the external application of cold. Ice to the surface, pouring cold water over the body, wrapping it in a cold pack, putting it in a cold bath, are the active means by which inhibition is stimulated and the hyperpyretic condition subdued in urgent cases. In cases in which the danger is less urgent a tepid bath or tepid sponging may suffice; but in all the principle is the same, the application to the surface of the body of water having a much lower temperature than the body. Where the temperature is very high and the danger very urgent, rubbing the body with ice or putting it in a cold bath till the temperature falls to 100°, is the most speedy means of attaining the desired end, care being taken not to cause too great depression. Where the danger is less urgent the desired end is sufficiently attained by keeping ice applied to the head, and by, at the same time, frequently sponging the body with cold or tepid water. A simple and efficacious plan is to keep flipping the surface of the body, now the chest and abdomen, now the back, and now the limbs, with a sponge slightly moistened with cold or tepid water; the sponge should be soft, of loose texture, not more than two inches thick, and four to six inches in diameter. A sponge of that sort is easily flopped lightly and rapidly up and down on the surface; the fanning action by which this is done aids the action of the cold water in producing the stimulant action on the peripheral extremities of the nerves by which the desired impression is conveyed to the heat-inhibiting centre; it tends also to promote heat-elimination.

The practice of treating fever by cold baths is an old one, which had fallen into disuse. The good results got from this treatment in hyperpyrexia led to its revival. If the high fever which has to be dealt with in hyperpyrexia could be thus cured, might we not also by the same agency arrest the more moderate disturbance of an ordinary pyrexia? Such was the train of thought. Natural enough, but founded on a fallacy. It assumes that the two morbid conditions are similar in nature, and that hyperpyrexia is an exaggeration of pyrexia. But they are essentially different in their mode of production: hyperpyrexia is of neurotic origin, dependent on impaired inhibition, while pyrexia (that of idiopathic fever at least, which is the form of fever chiefly dealt with) is of metabolic origin, dependent on increased production of heat. Its curing hyperpyrexia is no proof that cold can cure pyrexia. And experience shows that it does not; for though some German physicians tried to show that the course of

typhoid fever may be arrested by the cold bath, their results have not been confirmed or accepted by subsequent observers.

Judiciously used, however, cold is a valuable agent in the treatment of fever; for though it may not cure, it tends to alleviate some of the symptoms, especially those referable to the nervous system. Its mode of application—in other words, the dose administered—should vary in different cases.

In urgent cases of hyperpyrexia it should be given at once in full dose, that is, ice or ice-cold water should be applied to the whole surface. In cases in which fever runs high, but in which the stage of pyrexia is not exceeded—that is to say, when the temperature ranges from 104° to 106°—cold sponging of the body with ice to the head will generally suffice. In cases in which it ranges from 102° to 104°, sponging with water from 80° to 90° F. is enough. In cases in which it does not exceed 102°, cold as an antipyretic is not called for, but tepid sponging is grateful to the patient, and it is not improbable that its regular use may, by gently stimulating inhibition, prevent that function from failing, and neurotic pyrexia from being developed. Cold is accumulative in its action, and should not be unduly pushed; its use should be omitted when the temperature falls below 101°—to be renewed if necessary. But it should be borne in mind that the temperature often continues to fall for some time after cold has ceased to be applied.

The Relation of Rheumatism and Chorea.

Of the existence of some relation between rheumatism and chorea there can be no doubt. The observations of Bright, Begbie, Hughes, Burton, Brown, Sée, Roger, and others, have placed this beyond question.

Chorea is essentially a disease of the nervous system. Its characteristic symptom is irregular and uncontrollable muscular twitching and jerking.

For the explanation of such a symptom we turn, not to that part of the nervous centres whose derangement causes delirium, wandering, and such phenomena as were noted in connection with inflammation of the heart, but to that part of them whose function it is to initiate, control, and regulate movement—the motor centres. How the rheumatic constitution leads to disturbance of these centres is the question which we have to solve.

There are two views on this point: one that the choreic symptoms result directly from the disturbing action of the vitiated blood on the nervous centres; the other that they are directly due to a prior

affection of the heart—the rheumatic condition acting only indirectly through this.

The former view is that advocated by Begbie. "I cannot help coming to the conclusion that the simple and true view of the relation of rheumatism and chorea is to be found in the morbid condition of the blood, which is admitted to exist in the rheumatic constitution; and this explanation will apply equally to chorea occurring in individuals or families inheriting the rheumatic diathesis; to chorea occurring in connection with rheumatism, but without the cardiac complication; and to chorea associated with pericarditis or endocarditis or both; the inflammatory affections of the fibrous tissues, as well as the spasmodic affections of the muscles, and the derangement of the nervous system, originating in the same specific disorder of the circulating fluids." To this explanation of the choreic symptoms, there is the same objection that applied to a like mode of accounting for the nervous symptoms noted in pericarditis. If due to the morbid condition of the blood, they ought to be much more common than they are; for that is a cause which operates in every case of rheumatism. Occurring, as they do, only in exceptional cases, they are more likely to result from an exceptional cause than from one which operates so generally.

The view that the chorea is consequent on a prior inflammation of the membranes of the heart is that which has commended itself to most other observers. There is some variety of opinion, however, as to the sequence of events by which the one phenomenon leads to the other.

Bright thought that the choreic symptoms resulted from irritation transmitted from an inflamed pericardium or pleura along the phrenic nerve. This explanation might apply to cases of chorea occurring in connection with pericarditis or pleuritis; but is quite inapplicable to the numerous cases in which no such inflammation exists.

In more recent times the view has been advanced and ably advocated by Kirkes, Hughlings Jackson, Broadbent, and others, that it is to endocarditis rather than to pericarditis that we have to look for the explanation of the choreic phenomena. The theory is, that some of the particles of lymph effused on the surface of the valves get detached, enter the circulation, and cause embolic plugging of the minute vessels of the motor ganglia; and some pathological evidence has been adduced to show that the corpora striata and optic thalami have suffered in fatal cases of chorea. The actual existence of embolism, however, has not been demonstrated; and its occurrence as a cause of chorea cannot be regarded as more than hypothetical.

That such an event is possible, there can be no doubt; but if particles of fibrin are detached from the valvular surface it is difficult to see why the vessels of other parts of the brain should not be plugged, as well as those of the motor ganglia; and why the embolic particles should not sometimes get into other organs and give rise to infarctions of the lung, spleen, kidney, etc.

Again, if the cause of chorea in rheumatic subjects be the detachment of particles of lymph from the surface of a roughened valve, how are we to explain its occurrence in those numerous rheumatic subjects whose valves have never been affected? To such cases this embolic theory is quite inapplicable. It cannot, therefore, be regarded as adequate. Just as Bright's theory might apply to cases of chorea occurring in connection with pericarditis, so this one might apply to cases of chorea occurring in connection with endocarditis. The fault of each is its narrowness, and the impossibility of applying it to more than a minority of the total cases of rheumatic chorea. What we want is an explanation which will apply to all cases of that disease—those occurring in connection with pericarditis—those occurring in connection with endocarditis—those occurring in connection with simple rheumatism of the joints, uncomplicated by any heart affection—and those occurring in persons of rheumatic constitution but who, at the time of the choreic attack, are not suffering from rheumatism of either the heart or joints.

The theories hitherto advanced have given prominence to two different factors—the morbid condition of the blood, and the inflamed condition of the heart. Neither has been sufficient to meet the whole of the facts. A much wider pathological view is required for that purpose.

Rheumatism is essentially a disease of the motor apparatus; chorea is essentially a disease of the motor centres. In this broad pathological statement we have the clue to the explanation of the relation of the two diseases.

The motor centres affected in chorea, and the motor apparatus which suffers in rheumatism, have an essential physiological connection. The motor centres form the central portion of a system, of which the motor apparatus is the distal or peripheral. Each is essential to the physiological completeness of the other, and without the other neither has any physiological *raison d'être.* Without joints to be moved, the motor centres would be useless; without motor centres to initiate the necessary nervous force, the muscles would remain flaccid and the joints be of no avail.

The seat of chorea and the seat of rheumatism having so close a physiological connection, it need not surprise us to find that there is

some connection between these two diseases, and that those who are subject to the latter are also liable to have the former.

The existence of the rheumatic diathesis implies a liability to disturbance of the motor apparatus. The motor ganglia are an essential part of this apparatus. Those subject to rheumatism are, therefore, *cæteris paribus* more likely to have susceptible motor centres than those who are not. Thus the rheumatic diathesis predisposes to chorea. So much physiology teaches. But the practical questions still remain—How is the chorea induced; what is its exciting cause; and why does it occur only in a small percentage of the total number of rheumatic subjects?

Here, as is the case with delirium and nervous symptoms generally, constitutional predisposition plays an important part. The motor centres, like all other parts of the nervous system, are more susceptible and more liable to disturbance in females than in males, and in young people than in those of more mature years. We accordingly find that it is in females and in young people that choreic symptoms are most apt to show themselves. The rheumatic constitution is by no means necessary to their production. A fright, or nervous shock, gastric or uterine derangement, may give rise to chorea and be the exciting cause of the disease in persons in whom there is no history of rheumatism. But many cases there are—so many that the connection is too striking to have escaped detection—in which a present or prior rheumatic attack, with or without heart affection, is the only cause to which the chorea can be traced. Many cases there are, too, in which a rheumatic family history forms the only noteworthy feature.

In discussing the pathology of rheumatic chorea, we thus have two different classes of cases to deal with—those in which the chorea occurs either in connection with, or subsequent to, a rheumatic attack; and those in which there is only a family history of rheumatism.

A rheumatic attack means inflammation of an essential and important part of the motor apparatus and general disturbance of the whole system. If a nervous shock, or derangement of the digestive or uterine organs, may induce chorea in one predisposed to it, a rheumatic attack or an endocarditis may almost certainly do so too; for general rheumatic disturbance of the motor apparatus cannot but be regarded as a possible cause of disturbance of the motor centres. Thus the rheumatic diathesis may be the predisposing and the rheumatic attack the exciting cause of an attack of chorea. The combination of these two causes in the same subject suffices to explain the special tendency of chorea to occur in those who have suffered from

rheumatism. The heart complications, to which the choreic phenomena are by some ascribed, are a mere incidental accompaniment of the disease. They may, of course, act as an exciting cause in the same way as the joint affection or derangement of the uterine organs may, but they are not essential to the production of chorea.

But the predisposing cause may exist without the exciting. There may be a family predisposition to rheumatism, without the disease having ever occurred in a given member of the family. Choreic symptoms may show themselves in such a one without any prior rheumatic attack, the exciting cause being some other disturbing agency, such as shock or gastric or uterine disturbance. No matter what the exciting cause, the disease is fitly described as one of rheumatic chorea, if what tended to its production, and predisposed to its existence, was the rheumatic constitution of the individual.

In a rheumatic subject predisposed to chorea through a susceptible condition of the motor centres, it is an accident whether the chorea, when it does occur, comes on in connection with a rheumatic attack, subsequently to it, or prior to and independently of it. The ultimate pathological explanation of the relation of the rheumatism and the chorea is the same in each; the one disease consists in disturbance of the peripheral portion of the motor apparatus of the body; the other consists in disturbance of the motor centres.

In persons with susceptible and easily disturbed motor centres chorea may be induced by causes which would not give rise to it in others. The motor centres are most easily disturbed in people of rheumatic constitution because rheumatism is essentially a disease of the parts of the body over which the motor centres preside. Other morbid conditions, gout and rheumatoid arthritis, also affect the motor apparatus, without disturbing the motor centres; but then they occur at an age at which chorea does not manifest itself. Chorea is essentially a disease of youth—so is rheumatism; it is the only joint trouble which is so.

GOUT.

BY

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CHICAGO.

GOUT.

Synonyms.

In the writings of Hippocrates and Aretæus, gout is known as ἀρθρῖτις, a term derived from ἄρθρον, a joint, and ιτις, inflammation. As the foot was the most conspicuous seat of the disease, it was by these early authors frequently called ποδάγρη, or ποδάγρα, a derivative of the words πούς (*gen.* ποδός) and ἄγρα, signifying a disease or attack involving the feet. By some of the early Greek authors it was mentioned as ποδαλγία from πούς and ἄλγος, denoting and calling attention to the painful condition of the feet during the attacks of the disease.

From the Greek these terms were transferred without change into the Latin. Under the empire we find the terms *arthritis* and *podagra* in common use. Pliny mentions a *morbus arthritis*, under which he probably includes rheumatism as well as gout. The writers of the later Greek empire, taking their cue from the word *podagra*, amplified their terminology by coining such words as *chiragra*, from χείρ, the hand, and ἄγρα, a seizure, or attack; *gonagra*, from γόνυ, the knee; *omagra*, from ὦμος, the shoulder; *tenontagra*, from τένων, a tendon; *cleisagra*, or *cleidagra*, from κλείς, the clavicle; *odontagra*, from ὀδούς, a tooth; thus illustrating the pliability and the exuberance of the Greek language in its adaptation to the necessities of an expanding scientific literature. As these later terms came into use they were employed to indicate the particular species of the disease, while the word *arthritis* was used with increasing precision as the generic term to denote articular disease in general.

The disease did not escape the notice of the comic poets, who bestowed upon it various names that lie outside of the pale of science.

Its aristocratic relationship was recognized in the name *morbus dominorum*, by which it was known to Latin authors. The modern name *gout* first appears in its Latin antecedent *gutta*, a term that was employed by Radulphus, or Rudolph, who wrote in the later years of the thirteenth century. He taught that gout was a disease that was caused by a humor that flowed drop by drop, *guttatim*, into the joints. Hence the term passed into the different European languages, giving us *goutte* in French; *Gicht* in German; *gotta* in Ital-

ian; *gota* in Spanish. Other names have also been employed in different countries, by different authors. Among the early Saxon-English the disease was called *fotadl*, or *foot-addle*, that is, *foot-ail*. By the Germans it is known in the popular vocabulary as *Gliedersucht*, *Gichtschmerzen*, *Fussgicht*. Among the learned it has been known as *febris podagrica; podagra arthritis; arthritis uratica*, or *urica; pan-arthritis urica; arthrodania podagrica; cauma podagricum*, from καῦμα, burning; *arthrosia podagra*. Latent and irregular forms of the disease have been denoted by the terms *lithiasis*, and *lithæmia*, derived from λίθος, a stone, and αἷμα, the blood, having reference to the presence of lithic or uric acid compounds in the blood and tissues of the patient who suffered from the imperfectly developed varieties of the disease.

History.

It is impossible to assign a date beyond which gout was unknown. The treatises of Hippocrates describe the disease in unmistakable language. Upon the monuments of Egypt the gentry of that ancient country are depicted in the enjoyment of liberal vinous potations, with all the accessories that are provocative of arthritis.

We are told (1 Kings xv.) that, about nine hundred years before Christ, Asa, the king of Jerusalem, the great-grandson of Solomon, died of the gout. From that day to the present time, there are few of the monarchs and great men of the earth, who have not felt the twinges of the arch-enemy. To say nothing of Persian and Chinese and Japanese experience in that line, we find in the light literature of Greece and Rome frequent allusions to the over-weighted and irascible victim of podagra, who is vastly amusing to every one but himself.

Even among more serious authors, men of the world, like Seneca, complain of the luxury that had debauched the imperial Romans, so that even the ladies of the court were bald, and fat, and gouty by reason of the ardor with which they devoted themselves to the worship of Venus and Bacchus. History continually repeats itself; and wherever wealth and leisure abound, gout has embittered the lives of the votaries of pleasure. Nor have they alone been numbered among the victims of the disease. Many of the most eminent among the intellectual leaders of men have been, either as a consequence of their own errors or through hereditary predisposition, made to suffer in common with the princes of fashion and dissipation.

The famous John Milton, author of "Paradise Lost," in addition to the total loss of sight was a great sufferer with gout, which stiffened and deformed his fingers. His well-known contemporary, the indus-

trious Samuel Pepys, was from early life a martyr to the stone and to visceral gout.

Not alone, but perhaps most conspicuous among politicians, was the famous Lord Chatham, whose experiences with the protean forms of the disease have been so graphically described by Lecky in his "History of England during the Eighteenth Century."

From the dawn of English history till the premiership of Lord Beaconsfield, there are few of the prominent men of Great Britain who have not contributed their share to the illustration of the clinical course of the disease. In this work the medical profession is not without honor, for it was the learned Sydenham whose thirty-four years of experience with the disease enabled him to compose that description of gout which had never been equalled, has never since been surpassed, and is still a medical classic. At the early age of sixty-five his life was terminated by an acute attack of the disease with which he had so long contended.

As one reads the pages of history it is with painful interest that one remarks the manner in which many of the most precious lives were shortened and old age was tormented by the gout.

Allusion has been already made to the writings of Hippocrates. In his work "On the Prognostics" he says: "With regard to persons afflicted with the gout, those who are aged, have tophi in their joints, who have led a hard life, and whose bowels are constipated, are beyond the power of medicine to cure.

And among the Aphorisms occur the following:

"Eunuchs do not take the gout, nor become bald.

"A woman does not take the gout, unless her menses be stopped."

But when Celsus and Galen wrote, in the days of the Cæsars, luxury had risen to such a height that both women and eunuchs became bald and suffered with the gout. Hippocrates also notes the greater prevalence of gouty affections in spring and in autumn; and it was his opinion that the inflammatory symptoms by which they were accompanied subsided in the course of forty days.

These ancient authors scarcely distinguished gout from rheumatism, and for this reason Sydenham and others have conjectured that gout was more prevalent in ancient times, while rheumatism was a comparatively modern disease. But the examination of the bodies of the dead from the buried cities of Pompeii and Herculaneum has resulted in the discovery of the articular lesions of chronic rheumatism, thus proving a very respectable antiquity for that disease.

It is thought that Aretæus of Cappadocia, writing in the first century, had some perception of the difference between the two diseases when he asserted that "Pain that is prevalent in all the joints con-

stitutes arthritis; but pain in the foot is the characteristic symptom of what is called podagra." The same author appears to have been well informed regarding the etiology of the disorder, for he goes on to say: "The victims of the disease always ascribe it to a tight shoe, or to a long walk, or a blow, or some sort of pressure, but not one of them will acknowledge the real cause of his malady; and if you inform them that they have the gout, they pretend not to believe it."

The most complete and graphic description of the gout that has reached us from the early years of the Christian era has been usually attributed to Cælius Aurelianus, a Numidian physician who taught medicine in the city of Rome, about the close of the fourth century. He translated into Latin numerous volumes that had been composed in Greek by Soranus of Ephesus, a graduate of the medical school of Alexandria, and one of the most distinguished physicians in Rome during the reign of the emperors Trajan and Hadrian. His original works have been lost, and are only known by their translations, which have been often erroneously considered as the composition at first hand of their translator. Their real author was a fashionable obstetrician, and one of the immediate predecessors and rivals of Galen, yet he found time to become one of the most voluminous and highly esteemed medical writers of imperial Rome. His description of acute gout is as accurate and as vivid as the corresponding work of Sydenham. His companions and successors in the palmy days of the Alexandrian medical school were thoroughly familiar with the physiognomy of gout, and they endeavored to search out its remote causes, and to determine its pathogeny.

Alexander of Tralles advised bleeding, in order to reduce the local inflammation, and he employed as an internal remedy a plant (*hermodactylus*) that was probably allied to colchicum.

Aëtius and Paul of Ægina respectively noted the hereditary character of the disease, and the conspicuous influence of fatigue, debauchery, and drunkenness as exciting causes.

During the middle ages but little progress was made toward a comprehensive theory of gout. The over-rated Arabian physicians merely repeated what they had learned of the Alexandrian tradition.

But toward the close of the thirteenth century, a learned Greek physician, Demetrius of Pepagomenus, prepared for the benefit of his master, the Byzantine emperor Michael Paleologus, a summary of existing knowledge on the subject of gout. In this carefully wrought compilation the theories of Galen dominate the work, but the clinical picture of the disease is accurately drawn. Gout is represented as a general disorder with variable local manifestations, and its causation is ascribed to debility of the digestive apparatus, and an erroneous

mode of living. These factors lead to an overloading of the body with peccant humors that discharge themselves upon the articulations. Hence the prime importance of moderation and temperance as prophylactic measures. But this prescription, so easy to give, was in those days no more willingly accepted than in our own *fin de siècle*.

During all these centuries it is evident that the distinction between gout and rheumatism was not always kept clearly in view.

It was to the learned Baillou, who at the close of the sixteenth century stood at the head of the medical faculty in Paris, that must be credited the honor of establishing the differential diagnosis between the two diseases. A century later, Sydenham, in his classical essay, sharply defined the limits of the kindred articular inflammations, and studied in his own person the natural history of gout with the truly scientific spirit of the modern school.

The eighteenth century could add but little to the work of Sydenham.

Musgrave devoted an essay to the consideration of the metastatic and visceral forms of gout; and during the later years of the century, Cullen endeavored to account for the phenomena of the disease by reference to a supposed disorder of the nervous function.

Upon the continent, Boerhaave, van Swieten, Hoffmann, and Stahl wrote learnedly, but contributed very little to the advancement of knowledge of the subject. For many of the years of the seventeenth and eighteenth centuries it was believed that the concretions which hampered the joints of the gouty were due to a precipitate of "tartar" upon the articulations, this tartaric salt being derived from the ill-ripened wine that was consumed by the patient.

Sydenham was too far-seeing and too well-read in ancient lore to admit so crude an explanation. He taught the ancient doctrine of peccant humors that were thus eliminated from the circulation, but it was only through the process of chemical investigation that the true nature of the deposit was determined.

Wollaston and Tennant, in 1797, announced as the result of analysis that the concretions of gout consisted of sodium urate, a discovery that has led up to some of the most important of modern theories of the disease. In England the leaders of medicine during the nineteenth century—Scudamore, Prout, Holland, Forbes, Graves, Good, Todd, Watson, Duckworth, and especially Sir Alfred Garrod—have elaborated the doctrine of uric-acid intoxication.

In France the same views were accepted by Andral and Rayer in the earlier part of the century. Cruveilhier and the pathological anatomists made careful studies of tophi and the articular lesions. Ranvier, d'Ollivier, and Lancereaux have devoted much time to the

lesions of visceral gout; and in comparatively recent years Charcot has enriched the literature of medicine with his lucid descriptions of arthritic disease, while Bouchard and his pupils have done good service by emphasizing the diathetic character of the disorder.

In Germany, where gout is less common, the subject has been ably reviewed by Virchow, Senator, Erlenmayer, Seligsohn, Ebstein, and Pfeiffer. It is in England, however, that the subject is still investigated with the greatest interest. Latham, Roberts, and Haig are among the most recent students and observers of their national disease. To Haig, especially, belongs the honor of being the most recent, the most enthusiastic, and the most perspicuous of all the writers who have illuminated the subject since Garrod commenced the work that is being thus continued. Incomplete as much of his labor must be considered, it is based upon a correct method, and only needs extension to reach the most important results.

In America the conditions of life during the colonial period were unfavorable to extensive observation of the manifestations of acute gout: but with the settlement of the country and the growth of luxury the disease becomes more frequent in the centres of population.

The famous Benjamin Rush devotes a chapter to the subject; and the medical journals of the early part of the nineteenth century contain occasional references to exhibitions of the disease in the persons of stranded Europeans or Americans who had acquired European habits of life. But, with larger experience, it has become apparent that even among temperate Americans the irregular and masked forms of arthritism are not uncommon.

A whole literature of observations on this branch of the subject is in process of formation, and much that is interesting may be expected from this line of research.

Definition.

To formulate a concisely accurate definition of gout is impossible, for the reason that the disease is not a simple entity, but is both a local disorder and a general perversion of nutrition.

More than this—it is one of the most conspicuous manifestations of a particular diathesis. Gout belongs to that remarkable group of diseases in which the existence of an individual tendency on the part of the patient constitutes what is known as the arthritic diathesis.

By the term diathesis is signified not merely an hereditary or acquired predisposition, but a predisposition to certain related diseases. The particular diseases that are grouped in the arthritic class are not so much related by location and community of symptoms as by the fact that they are, in some way that is not yet fully comprehended,

connected with a disorder of nutrition which hinders the process of oxidation in the tissues. As a consequence of imperfect oxidation the liquids and the solids of the body become charged with products which represent, not the ultimate results of perfect oxidation, but rather the intermediate steps of the process. Instead of water, carbonic acid, and urea, as the only terminal products, there is an excessive formation of uric acid, fat, and the fatty acids; and sometimes there is a surplus of unoxidized sugar which is ejected as an unprofitable excretion. From the earliest ages this diathetic characteristic has been noted by every observer of gout, until it has become a settled conviction that gout is only a special manifestation of a tendency which, modified by the varying conditions of life, results now in one, and again in another, of the different diseases that are united in the arthritic diathesis.

Their close relationship is still farther illustrated by the fact that the same patient may sometimes experience a number or all of them, either successively, alternately, or at the same time.

Thus it is not an uncommon clinical experience to witness in the same subject the simultaneous occurrence of baldness, pityriasis, eczema, varicose veins, hemorrhoids, asthma, chronic catarrhal inflammation of the mucous membranes, neuralgia, and some form of irregular gout or chronic rheumatism. Sometimes it is obesity and gout or diabetes that are thus associated. Sometimes obesity exists in one generation, and is followed in the next by diabetes or by the gout; and the converse may also be witnessed.

Gout is, therefore, one of the forms in which the arthritic diathesis may be individualized. But it is not merely a local disease of the joints marked by specific lesions. Nor is it only a general consequence of an excessive accumulation of uric-acid compounds in the body. It is all this, and something more. It includes also the perversion of nutrition—a perversion that does not proceed at random, but is based upon recondite constitutional peculiarities which may have been either hereditary or acquired, and are in conformity with certain, as yet undiscovered, processes of molecular chemistry.

We know that these processes may be induced by errors of diet and insufficient muscular exercise, but we do not know in what they ultimately consist. Three facts must therefore be considered in connection with every example of gout: 1, The diathesis, with all its racial and constitutional affiliations; 2, the chemical condition of the blood, overcharged with imperfectly oxidized compounds of nitrogen; 3, the local effects of the precipitation in and about the joints and other structures of such nitrogenous compounds, typically represented by sodium urates. These three factors may be all associated in the

same individual; or one or more may be suppressed, giving origin, in the first place, to complete and typical examples of the disease, and to atypical, undeveloped, and irregular forms when suppression of certain fundamental characteristics has occurred. Thus, in the majority of acute cases of the disease, it is comparatively easy to demonstrate the diathetic peculiarities and tendencies of the patient. It is also an easy matter to find urates in the blood, and to note the local injury that results from infiltration of the joints and other tissues with the mineral deposit. Such cases constitute the regular, typical form of gout.

But in many instances it is impossible to discover the local lesions that were just now indicated, and it is difficult to find uric-acid compounds in the blood; yet the arthritic diathesis may be sufficiently conspicuous through the occurrence of disorders that belong to the arthritic group. It is, therefore, necessary to be familiar with their physiognomy in order to medicate them successfully, and to forewarn the patient against evils to which he is liable, if he depart from the necessary regimen. Such patients, though they may never have suffered with articular inflammation, are subject to paroxysms of hemicrania, or asthma; they often exhibit patches of erythema and eczema; they are familiar with varicose veins, hemorrhoids, enteralgia, gastralgia, neuralgia of the heart and precordial nerves, dry and spasmodic cough, sneezing, acid dyspepsia, depression of spirits, insomnia, neurasthenia, all of which are determined by the permanent existence of the arthritic predisposition, and are allied by that common factor, as well as by their frequent alternation with the regular variety of the disease. Sometimes, especially as the years progress, the regular form of gout, by which the patient had been afflicted in earlier life, becomes suppressed, and in its place appear these irregular forms of the disease. Such abarticular manifestations are usually termed irregular gout, not because they furnish less characteristic exhibitions of arthritism, but because of their irregular incidence, coincidence, and sequence.

By the older physicians these forms of gout were often described as latent, suppressed, displaced, or metastatic cases of the disease. They are sufficiently indicated by the term *irregular* as contrasted with regular gout.

It is often convenient to speak of gout as being either acute or chronic. This division has its foundation in the fact that the paroxysm of regular gout is usually very severe, is attended by acutely inflammatory symptoms, runs a rapid course, and may be followed by a long intermission with freedom from painful disorder.

But in too many instances an acute attack may subside into

chronic misery, in which the use of the terms acute and chronic is impossible without considerable confusion of ideas.

Besides this, it must never be forgotten that, no matter how short and sharp the paroxysm, the predisposition upon which it rests is a chronic and permanent condition of ill-health.

Without attempting to give a definition that shall rise above criticism, we may, therefore, speak of gout as the most conspicuous manifestation of a predisposition that is either hereditary or acquired, and is in both cases permanent during the remainder of life.

The disease may be either acute or chronic in the fluctuations of its course; regular or irregular in its evolution.

Characterized, in acute and local varieties of the malady, by infiltration of the articular structures with compounds of uric acid, the tissues of the entire body may be finally either directly or indirectly ruined by kindred errors of nutrition. The progress of the disorder is marked by disturbances of sensation, motion, secretion, excretion, and nutrition that in acute cases reach the level of active local inflammation accompanied by painful swelling, heat, and fever.

Morbid Anatomy.

The deformation and destruction of the joints that take place in chronic gout furnish a picture with which the earliest of investigators were only too familiar. The ancient writers were careful observers, and many of their descriptions of the macroscopic appearance produced by the disease are as perfect as anything that has since been recorded. The chalky deposits that infiltrate the joints were, however, regarded as something uncommon, and only to be found in chronic and inveterate cases of the disease. They were supposed to represent the "peccant humors" that filtered drop by drop into the cavity of the affected joint, until it could hold no more, and overflowed into the adjacent tissues.

The great merit of Sir A. Garrod's researches lay in his demonstration of the fact that the urates, which compose the bulk of these deposits, were not absent from the articular tissues in cases of acute and recent gout—even when no external evidence of infiltration could be detected. To his investigations is due the proof that in every case of articular gout uratic infiltration is the primitive and all-important fact.

When a gouty joint from a patient in an early stage of the disease is laid open for inspection, the first thing that fixes the attention is the change that is exhibited by the diarthrodial surfaces. Instead of the uniformly smooth and yellowish-white surface presented by the

cartilaginous investment of healthy bones, there are visible, here and there, stains and streaks and spots of a dull clayey-white, imbedded in the substance of the cartilages. The superficial layer of pavement cells is not involved at this early period of infiltration, and the articulation still retains its normal shape and function. But as the disease progresses the process of infiltration advances, until the entire cartilage at the end of the bone is transformed into a uniformly clayey-white substance occupied by a deposit of sodium urate. The superficial layer is now attacked, and the articular surface becomes roughened by the destruction of the endothelial layer.

These erosions become deeper and wider, and irregular protrusions of inflammatory tissue that has become saturated with urates encroach on the cavity of the joint. In aggravated cases the original diarthrodial structures disappear, and the roughened ends of the bones project into an irregular cavity that is filled with a semifluid substance that resembles a mixture of plaster-of-Paris and water before it has solidified. The capsule of the joint and its component ligaments and tendons are also in like manner saturated with mineral matter, which is sometimes thus accumulated in great quantity, to the utter deformation and ruin of the affected part.

The location of this morbid process is not an accidental affair. The small joints of the extremities are the favorite points of attack. The frequency with which the articulations of the great toe are invaded in cases of typical gout has always arrested attention. Next in order come the metatarso- and metacarpo-phalangeal articulations; then the joints at the ankle and the wrist.

The larger articulations of the upper and lower extremities, and of the vertebral column, are less liable to invasion, and when they suffer, the progress of the disease from the periphery toward the centre is less regularly marked. Occasionally, however, some of the large joints are diseased, while the smaller joints of the hand and wrist remain entirely free from infiltration. As a general rule the extent and the severity of the lesions are proportionate to the frequency and the intensity of the local attacks of the disease; but sometimes it happens that post-mortem examination reveals characteristic changes in articulations that had never been suspected of disorder during the life of the patient.

An interesting fact that may be noted in this connection is the manner in which the diarthrodial infiltration progresses. It is not at the periphery of the joint that the characteristic clay-colored spot appears at the commencement of the process; it is in the central portion of the cartilaginous expanse that the primitive lesion is discoverable. Here is the most conspicuous area of change, while the

peripheral portions of the articular surface exhibit only insignificant streaks and spots of disease. Since the regions thus primitively involved are the farthest removed from the network of nutrient capillaries that feed the diarthrodial structures, it is highly probable that the cause of this selection lies in the comparative absence of circulation and the more easily retarded nutrition that must characterize such territories. It is also probable that the direct effect of superior pressure upon certain portions of the cartilages may act as a determining cause. The well-known fact that a gouty attack may be precipitated by a long walk, a dance, or any other event that necessitates unusual compression of the joint surfaces, lends additional color to this hypothesis. Wherever circulation and nutrition are retarded, a crystalline deposit of sodium urate will be more easily effected. For this reason the process of infiltration is at an early period manifested at the points of insertion of the lateral and inter-articular ligaments; so that when the joint is laid open the clay-like deposit that occupies the centre of the cartilage is separated by a considerable healthy space from the streaks and smaller patches that mark the ligamentous structure in the capsular wall of the articulation.

Thus far, the process is one of simple infiltration, analogous to the gradual calcification of tissues that takes place in the bodies of the aged. In this way the large ligaments of an affected joint, like the knee and ankle, may in the long course of the disease become transformed into completely petrified bands and cylinders which only by their position serve to indicate the healthy tissue in which they originated. Such utter destruction, however, is not so conspicuous in the capsular ligaments as it is in the large crucial ligaments of the knee and in the structure of the ankle and wrist; and it is only in very inveterate cases that time is afforded for its complete development.

In like manner with the cartilaginous and ligamentous structures, the synovial membranes and their fringe-like processes are invaded. At first, the delicate serous surfaces appear as if dusted over with finely powdered plaster of Paris; but close inspection shows that the deposit is not upon the surface but is laid down in the subserous tissue. This indicates that, as in the cartilages and probably everywhere, it is an interstitial deposit that takes place instead of a superficial precipitation of foreign matter. The condition of the synovial fluid is somewhat variable. In old cases that have suffered severely and have experienced great articular disorganization, the fluid contents of the joint become turbid, thickened, sometimes acid, and looking like thin mortar. This appearance is due to the presence of urate of sodium in the form of fine particles like dust that can be

recovered from the desiccated liquid. But, more frequently, when the cartilages have not been disorganized by ulceration the synovial fluid exhibits little, if any, change. Sometimes, however, there is almost total absence of the lubricating fluid, though the small amount that is present retains its ordinary qualities, and contains no mineral matter in suspension. The acid reaction of the synovial liquid that has been above noted is not of frequent occurrence.

Even after considerable lesions of the joints it is usual to remark a neutral or alkaline reaction on the part of the articular contents. It is probable that these differences depend chiefly upon the extent to which the joint surfaces have become incrusted with a uratic deposit. So long as that deposit is inconsiderable and does not invade the serous cells that elaborate the synovial fluid, so long will the liquid contents of the joint retain their normal reaction and appearance. But when the serous membrane has been invaded by the mineral incrustation, as its cells become detached, they carry with them a contribution of sodium urate by which the constitution of the liquid is finally transformed.

By the process above described it is evident that great changes must be effected in the articular structures. But the deposits of mineral matter that are thus formed do not remain inoperative in the way of farther change. By their presence they interfere mechanically with circulation and nutrition. They serve to irritate the nervous filaments with which the articular tissues are more or less richly endowed. Consequently, the phenomena of irritation are soon manifested, and, through the influence upon the nervous system that is thus originated, nutrition is further impaired. Even in mild cases, before the joint surfaces are injured, microscopical examination of the cartilages in which interstitial infiltration has begun shows that inflammatory action is evident in the immediate vicinity of the foreign matter that has been thus intruded into the diarthrodial substance.

It is in the cartilage that the process of inflammation begins. Here a double action may be observed: proliferation and necrosis of cartilage cells. In the central portions of the joint the process of necrosis is most conspicuous. Inflammation rapidly leads to cellular atrophy, and the uratic deposits are thus laid bare so that by erosion they are worn down, and their substance is washed away into the cavity of the joint. With the extension of the deposit, the process of atrophic inflammation and erosion keeps pace, until the ends of the bones are worn out of all semblance to their original structure.

While this atrophic process gradually erodes the bearings of the

joint, a different state of nutrition obtains along the borders of the cartilage. Here the deposits are relatively small, and the tissues are relatively rich in capillary vessels. Consequently, the inflammatory process results in a more luxuriant cell-growth; the cartilage cells break up and are replaced by embryonal forms; the marginal structures of the articulation become thickened by the growth of what are known as *ecchondroses*, which are simply masses of proliferating cells originating in the normal cartilages near the insertion of the synovial membrane, where there is an abundant circulation of nutrient fluids. The free surface of the joint in consequence of this process loses its natural polished appearance, becomes rough and irregular; while the normal elasticity of its fundamental substance is exchanged for a brittle and earthy fragility.

The elaborate transformation above described is chiefly notable in the large joints such as the knee and the ankle. In the smaller articulations of the toes and fingers, the destructive processes are more uniform, and the ruin of the joints is more complete. Cartilages and synovial membranes disappear beyond recognition, and the ends of the bones are plastered together with a mortar-like incrustation that produces complete ankylosis and immobility of the joint. In some cases the central cavity still retains some moisture, but in many instances all the parts of the articulation, and even the adjacent tissues for a considerable distance outside of the capsule, are solidly infiltrated. This may occur in cases where no dislocation nor deviation of the phalanges nor any swelling of the joints can be perceived.

The degree in which the true osseous structures behind the diarthrodial cartilages escape the destruction that ruins the softer tissues is remarkable. In the vicinity of the larger joints the epiphyseal portions of the long bones sometimes appear unchanged, though the articulations are profoundly altered by disease. Usually, however, the bone shares in the morbid process.

A certain amount of osseous swelling can be demonstrated as the result of chronic osteitis. The central spongy portion becomes more spongy and vacuolated, while the peripheral parts are condensed and eburnated by the infiltration of ordinary earthy salts.

Unlike the cartilages the bones almost never contain uratic deposits. In a few very exceptional cases which were observed by Féréol and Sir Alfred Garrod, the diarthrodial extremities had been destroyed, and certain little pockets in the bony substance were filled with a deposit that was continuous with the intra-articular incrustations. In only one instance did Féréol find the diaphysial portion of a single phalanx actually infiltrated with urates.

The periosteum, on the contrary, by reason of its fibrous charac-

ter, shares in the predisposition manifested by similar articular tissues to become the seat of an abundant uratic deposit.

In the majority of cases, then, it appears that the osseous changes consist in a chronic inflammation that rarefies the spongy portion of the bone, and leads to an increase of fatty matter in its substance, due to fatty degeneration of the osteoplastic cells; while the external portion of the shaft becomes eburnated and enlarged without uratic infiltration. Occasionally the lesions of arthritis deformans are found coexistent with those of gout. This is especially true of the smaller joints, which are sometimes surrounded by osteophytes that have formed in the marginal structures. These growths, however, are not characteristic of gout, for they do not consist of urates, and they may be encountered in other forms of arthritis.

By the aid of the microscope the infiltrative process is made still more conspicuous. The crystalline forms of sodium urate are rendered visible, so that the dust-like deposits and the clayey streaks and patches which seem to incrust the cartilaginous surfaces can be seen to lie beneath the serous investment. Fine lines of needle-like forms can be traced far into the substance of the cartilage, radiating usually from a central mass of crystals that looks opaque and homogeneous by reason of its condensation. It seems probable that these minute structures are at first deposited in the substance of the cartilage cells.

It is, moreover, certain that the fundamental substance of the cartilage is also occupied by the same crystalline deposit; but whether the process goes on simultaneously or successively in these two structures, cannot be positively determined at present.

When the irritation excited by the uratic deposit reaches the grade of inflammatory action the nuclei of the cartilage cells multiply and revert to their embryonal state. The superficial layers thus crowded with chondroplasts of recent formation become organized by an arrangement of cellular elements in rows parallel to the diarthrodial surface. The corresponding layers that lie contiguous to the bone allow their proliferating elements to range themselves in lines that are perpendicular to the osseous substance; while the intermediate layers lie at random without any attempt at linear order. At an early stage of the process the joint surfaces exhibit merely an absence of their normal polish, but with the progress of the disease the fundamental substance of the cartilage splits up, giving it a velvety appearance. At a still later period all the phenomena of erosive inflammation and mineral incrustation may be observed.

In the articular ligaments and synovial structures the same course of events may be studied. The process begins with a subserous de-

posit of mineral matter, and everything else follows as in the cartilaginous structures.

The secondary inflammation is less conspicuous than it is in the diarthrodial substance, but there is a similar proliferation of embryonal cells that insinuate themselves among the fibrous elements of the synovial membrane, and bud out into little adventitious growths that sometimes undergo fatty degeneration.

Outside of the joints the deposits of urates may occur in many different structures of the body, but everywhere the process is the same; it follows the same course and is accompanied by the same secondary events. In the neighborhood of the affected joints, especially those of the feet and hands, the periosteum, the ligaments, and other fibrous tissues become incrusted with uric-acid salts, adding to the deformity and bulk of the tophi that form upon the joints themselves. The tendinous sheaths also become similarly involved, especially those of the deep and superficial flexors of the fingers, and of the peroneal muscles and the tendo Achillis.

The various bursæ are very generally invaded. Their cavities are greatly distended, and are occupied with a more or less ropy or semisolid liquid that exhibits every stage of mixture with uric salts. Sometimes their contents are stained with exuded blood, or are semipurulent from infection with pyogenic bacteria.

In their order of invasion the bursæ upon the great toe and the metatarsal joints stand first; then follow those about the heel, the olecranon, and the knee. It is not usual to find evidences of disease in the bursæ elsewhere.

It is in these inflamed bursæ that is started the infective process that sometimes extends to the adjacent articulation, and results in purulent inflammation and complete destruction of the infected joint. It is not an uncommon thing in old cases of gout to be able to trace this process through all its stages, from incipient bursal inflammation, through perforation of the articular capsule, to final suppuration and ulceration of the infiltrated and incrusted tissues.

Another favorite place for a deposit of uric salts is in the subcutaneous connective tissue. Here they accumulate in patches under the skin, sometimes following the course of a tendon or muscle, usually movable, though more or less thoroughly adherent to the under surface of the skin. In such cases, the meshes of the deep layer, the Malpighian network, become infiltrated with urates which accumulate in little islets that are separated by fibrous bands.

The nutrition of the skin is necessarily hindered by this incrustation, and the integument becomes dry, earthy, and variable in thickness. Some observers have thought that the process began in the

sudoriparous glands, but analogy seems to contradict this view, since the glandular periphery is rich in capillary vessels, and infiltrations elsewhere affect non-vascular tissues by preference. In advanced cases the skin becomes inflamed, ulceration takes place, and there is established an obstinate sore from the surface of which exudes a mixture of blood and pus and uratic salts. In this way the integument may be extensively undermined, and fistulous passages opening into the joints may be excavated.

Small cutaneous tophi are frequently encountered upon different regions of the body, and they can be often recognized at an early stage of gout, even before the joints have been invaded. They have been carefully studied by Charcot and by Garrod who found them in nearly half his cases. They are usually of the size of a grain of wheat, but they sometimes reach the dimensions of a pea. They are exceedingly persistent, and they may excite the processes of inflammation and ulceration in the surrounding tissue like tophaceous concretions elsewhere. Their favorite seat is in the external ear, along the helix, or in the fissure that separates the helix from the anti-helix—less frequently in the anti-helix or upon the inner surface of the concha.

Somewhat similar concretions are to be found in the skin upon the palmar surfaces of the fingers. Ulceration followed by formation of indelible scars is a common event.

Other cutaneous deposits are occasionally discovered in the eyelids, in the alæ of the nose, and upon the cheeks, in the skin that covers the ulnar border of the forearm, and the internal aspect of the tibia. Sometimes concretions of various size are found in the integument, or in the subcutaneous areolar tissue of the glans penis or of the cavernous portion of the organ. Occasionally they exist in the deep tissues of the cavernous substance itself.

It is worthy of note that wherever these abarticular tophi are found, they are always related to the connective fibrous elements of the affected structure. Everywhere the parenchymatous, muscular, and glandular tissues escape, while the fibrous elements attract to themselves the infiltrating urates.

Chemical Characteristics of the Tophi in Gout.

Scheele in 1776, Tennant and Pearson in 1796, and Wollaston in 1797, demonstrated the existence of uric acid in the concretions of gout. Since then, a number of analyses have been made by physiological chemists. The results obtained by Laugier, Wurzer, and Lehmann are given in the following table:

	Laugier.	Wurzer.	Lehmann.
Sodium urate	25.92	29.70	52.12
Calcium urate	15.75	29.30	1.25
Sodium chloride	16.70	18.00	9.80
Potassium chloride	....	2.20	....
Calcium phosphate	....	....	4.32
Animal matter	16.70	19.50	28.49
Water Undetermined residue	16.60	10.30	3.88

Lehmann's specimen was taken from a metatarsal tophus, and it is probable that it included a fragment of bony substance. When an unmixed specimen can be obtained, it usually consists almost exclusively of the salts of uric acid. These can be easily recognized by the following reaction:

1. Treated with dilute hydrochloric acid there is no effervescent escape of carbonic acid gas; consequently calcium carbonate is not present.

2. Treated with nitric acid the tophus dissolves. The solution should be evaporated in a porcelain capsule to one-third its volume, when, if uric acid be present, a yellowish deposit appears, and, on addition of a few drops of ammonia, exhibits a rich purple color. This is known as the murexid test, and it affords a very accurate method of demonstrating the presence of uric acid.

3. If a tophaceous fragment be calcined in a capsule, the presence of animal matter will be indicated by the characteristic odor. Treating the alkaline residuum with a solution of silver nitrate, the abundant precipitate of silver chloride testifies to the presence of chlorides, which may be further shown to be in combination with sodium.

4. If a preparation be placed under the microscope and treated with a drop of acetic acid, it is possible to view the solution of the urate of sodium, and the precipitation of uric acid crystals upon the surface of the glass slide.

By these tests it is always possible to distinguish a uratic deposit from masses of merely calcified tissue. In the examination of abarticular and visceral lesions, this discrimination sometimes becomes a matter of importance, as will become evident in the study of the

Visceral Lesions of Gout.

The most important of these are the changes that are produced in the kidneys, of which the granular or gouty kidney furnishes the type. Usually surrounded with masses of fat that are adherent to its cap-

sule, the kidney is reduced in size, and its capsule appears thickened, with an unevenly warty surface due to retraction of the fibrous trabeculæ within the substance of the organ. Small cysts frequently protrude beneath the capsule, and they may be easily recognized by their translucent envelope. Owing to the adhesions that have grown up between the fibrous trabeculæ of the organ and its investment, it is difficult to peel off the capsule; and the attempt usually results in considerable laceration of the true renal surface. An incision carried through the kidney exhibits very decided reduction in the thickness of the cortex, so that it is sometimes reduced to a mere capsular investment of the tubular and pyramidal portions. This part of the organ is less atrophied, but the tubules are spread apart by the injected vascular tissue and the intense hyperæmia in the vessels that surround the pyramids. The walls of the renal pelvis are thickened and congested; its cavity is usually dilated, and is often compressed by outside masses of encroaching fat.

Microscopical examination reveals in the cortex an extensive proliferation of connective tissue, by which the convoluted tubules are crowded apart; the glomeruli are contracted, and their thickened capsules are fused with the surrounding connective tissue, while the vascular loops and tufts within their cavities exhibit the characteristic changes that are due to peri-arteritis. Among the uriniferous tubules, some have yielded to the pressure of the contracting fibrous elements, and have disappeared; the majority of them are reduced in calibre, and exhibit evidence of atrophy, though still conserving their normal epithelial lining. In a word, the histological changes are those which are characteristic of ordinary interstitial nephritis. The only pathognomonic sign that is usually present in the majority of gouty kidneys is the appearance of uratic crystals or concretions. These must not be confounded with the uric-acid crystals and concretions which are commonly found in the renal pelvis and tubules of calculous patients. It is true that gouty subjects may become calculous, and then the kidneys may exhibit a mixture of uric-acid and uratic deposits; but in the uncomplicated gouty kidney uric acid is only present in combination with a sodic or calcic base. It is then encountered, not in the secreting apparatus of the organ, but in its excretory structures, in the pyramidal portion. Here may be discovered a deposit of amorphous urates apparently occupying the lumen of the uriniferous tubules, and becoming visible as fine, white striæ that follow the course of the excretory ducts. Careful microscopical examination, however, renders it evident that these deposits do not lie within the tubuli, but that they encumber the fibrous tissue between the uriniferous tubules which still remain pervious to liquids. Here,

then, the uratic deposit follows the same law that was observed in the infiltration of the articular structures.

The vascular structures of the kidney are not always invaded by disease, but it is highly probable that in the majority of advanced cases their walls are involved in the sclerotic process.

Ebstein reports a case in which the renal papillæ had ulcerated as a consequence of the encroachment of tophaceous deposits. This must be a rare event.

Mention has been already made of the multiple cysts which so frequently abound in the renal substance. These are sometimes very numerous, and their magnitude may cause the almost complete disappearance of renal tissue. The capsule of the kidney may then enclose a number of contiguous though separate cysts. Their contents are subject to considerable variation of color and consistence, being sometimes clear and colorless like water; or sometimes pigmented and jelly-like. The pelves of such kidneys frequently contain calculi of various sizes and shapes; and similar concretions are sometimes found in the cystic vacuolations that have replaced the renal substance. The concurrence of these concretions with the characteristic articular lesions of gout serves to indicate the intimate relationship that associates gravel, calculous kidneys, and arthritic disease of the joints.

Amyloid degeneration of the kidney is occasionally connected with uratic deposits in the organ. Ebstein and others have reported a few cases of this kind. The same authors have also observed numerous instances in which extensive incrustation of the joints was unaccompanied by any trace of uratic deposit in the kidneys. Only the lesions of chronic interstitial nephritis were present, indicating that chronic inflammation, rather than mineral infiltration, is the fact of prime importance in visceral gout.

The circulatory apparatus stands next to the kidney in the order of incidence of visceral gout. The heart is scarcely ever found, after death, in a perfectly healthy condition. It usually presents in milder forms of the disease the characteristic ventricular hypertrophy that is associated with the contracted kidney, chiefly involving the left side of the organ. The valves exhibit very little change. The muscular substance of the heart frequently shows a sclerotic change; but sometimes it is absent even in cases of considerable hypertrophy.

But when gout has become inveterate, and the joints and kidneys have become infiltrated with urates, the heart exhibits dilatation of all its cavities. The muscular fibres present the appearance of granular degeneration with partial loss of striation. The entire organ is soft and flaccid; its walls are covered with fat that often penetrates between the fibres of the ventricular wall. The valves rarely show any

signs of disease; their discoloration is dependent upon post-mortem imbibition; and if diseased they are covered with vegetations, or have undergone calcification as in ordinary cases of endocarditis. Very seldom indeed is the discovery of true uratic deposit upon the cardiac valves, yet such an event has been occasionally noted. In like manner, the arterial walls hardly ever fail to present extensive atheromatous deposits, but are only in the most exceptional cases invaded by the true uratic infiltrations. The large vessels near the heart and the cerebral arteries are the favorite seats of degeneration. The inner coat and the muscular layer of the arterial wall become calcified, while the adjacent parts undergo fatty degeneration. By these processes the vascular walls lose their elasticity, and the lumen of the vessels is diminished or wholly obliterated. Sometimes ulceration occurs around the atheromatous patch, and thrombosis may ensue, with consequent liberation of emboli and obstruction of distant regions of the circulatory apparatus. These facts are of prime importance in explanation of the proclivity of gouty patients to diseases of the brain and to cardiac angina dependent upon interference with the vascular supply of those organs.

The veins present in a minor degree the same lesions that have been noted in the arteries. Sometimes they exhibit the clinical phenomena of phlebitis, but as this usually terminates in recovery, little is known about its anatomical changes. Occasionally a deposit of urates has been found in the wall of a vein, even though the arterial walls were not correspondingly affected, but this is a very rare event. Varicosity of the veins, on the contrary, is one of the most common evidences of the arthritic diathesis. Few are its subjects who do not sooner or later display this proof of the morbid condition of their venous system. Hemorrhoids, varicocele, varices, phlebitis, or periphlebitis, obstinate ulcerations dependent upon those conditions, and the chronic œdema so frequently involving the extremities of the gouty, are among the most common consequences of veno-vascular arthritism. The capillary network does not escape the general morbid tendency. Though not the seat, perhaps, of coarser infiltration, the frequent occurrence of capillary hemorrhages in different tissues of the body is sufficient to show that these minute vessels share in the universal deterioration of structure and function that characterizes the progress of gout.

In the respiratory organs, it is sometimes possible to discover uratic deposits in the bronchi, but this is an unusual incident. More frequently the fibrous structures and articulations of the larynx are thus invaded. The mucous membrane escapes, but the subjacent fibrous tissues are sometimes distinctly infiltrated with urates. Yet,

though it be not liable to such deposits, the mucous membrane of the air-passages is exceedingly prone to infiltration that is modified if not directly caused by the arthritic predisposition of the subject. Such patients in early childhood are subject to long-continued attacks of severe bronchitis; as infants they are wheezy; and as they advance in years their lungs become emphysematous. The bronchial mucous membrane is thickened and darkly congested; the bronchi are often dilated; the air cells of the lungs are greatly enlarged, and their walls have lost their elasticity. In old cases that have succumbed to failure of the heart, the lungs are engorged with blood and other liquids. Catarrhal or interstitial pneumonia is sometimes present; and this last affection is accompanied by thickening and adhesion of the pleural surfaces. The lymphatic vessels sometimes share in the inflammatory process—occasionally even to the extent of suppuration.

The digestive organs do not so conspicuously exhibit lesions that can be directly attributed to gout, yet their morbid changes contribute to the suffering of the patient, and often hasten the fatal termination of his disease. The liver most frequently exhibits the appearance due to chronic congestion. The capsule is thickened, and the peritoneal surface is often adherent to adjacent surfaces. The lobules are surrounded by zones of pigment, and their vessels are dilated. When the heart fails the central vessels are engorged with stagnant blood. When there is a marked tendency to obesity, the organ is pale, soft, and fatty. Sometimes the degenerative changes due to cirrhosis are present, and it is often difficult to decide whether the condition of the hepatic tissue is due to gout or to alcohol which has so long constituted the favorite beverage of the patient. Judging from analogies furnished by the condition of the joints, kidneys, and heart, it seems reasonable to believe that the fibrous tissue of the liver may be, like that of those organs, directly affected by the arthritic disease.

The stomach presents no specific lesions that are peculiar to gout. Its mucous lining is almost always in a state of chronic inflammation, but this can be usually explained by the dietetic errors of the patients in the matter of food and drink. Sometimes, when the kidneys are extensively diseased, the gastric membranes show an unusual vascularity and irritation caused by frequent vomiting and hæmatemesis of uræmic origin.

The intestines seldom exhibit any characteristic lesions, though in rare instances the villi have been found infiltrated with sodium urate. Usually, when any morbid appearances are discovered they are due to uræmic ulceration, or to accidental causes.

The brain is often diseased in fatal cases of gout, but seldom does

it display anything that is characteristic. Diseased vessels, hemorrhage, softening, degeneration of the cerebral substance—all these changes may be due to old age, or syphilis, or alcoholism, so that it is difficult to decide how far gout contributes to the actual disorder. Uratic concretions very seldom form in the brain, but they have been occasionally found upon the meninges of the brain and spinal cord, and upon the spinal nerve sheaths. Sometimes the cerebro-spinal fluid contains crystals of sodium urate. But it is always in the fibrous tissue that participates in the formation of the nervous envelopes that the deposit is found. Thus, it is in the sclerotic coat of the eye—fibrous envelope of the retina—that uratic concretions are occasionally discovered, while the other tissues of the organ escape invasion.

Changes of the Blood in Gout.

The existence of "peccant humors" in the blood was always suspected to be the cause of gout, and the discovery of sodium urate in the tophi gave a great show of probability to this hypothesis. When in 1848 Sir A. Garrod demonstrated an excess of uric acid in the blood of the gouty, one of the most important advances in our knowledge of the disease was made. Garrod most ingeniously substituted for the tedious chemical research of the laboratories a simple method of examination that could be performed by any one at the bedside. Having drawn a small quantity of blood with a lancet or a cupping-glass, the serum is separated after coagulation of the mass, and is placed in a watch-crystal or small porcelain capsule. Six drops of 28-per-cent. acetic acid are then added to every drachm of liquid, and a few threads of lint are immersed in it. All the water of the serum is allowed to evaporate, and at the end of twenty-four hours, or more, microscopical examination of the dried threads finds them covered with rhombohedral crystals of uric acid. A control specimen procured from the serum of a healthy person shows nothing of the sort. A similar result will be obtained if the serosity of a blister be treated in the same way. It is important to evaporate the serum at a temperature that does not exceed 70° F., for if the process goes on too rapidly crystals will not form.

If fermentation take place in the liquid, it becomes covered with a pellicle of ammonio-magnesian phosphates that get entangled with the threads and conceal the uric acid crystals. The earthy precipitates, however, readily dissolve in pure water, and by their disappearance unmask the insoluble uric-acid deposit. Fermentation may cause decomposition of the acid crystals, resolving them into oxalic acid, urea, and allantoin.

It is necessary, when procuring blood or serosity for this experiment, to avoid the neighborhood of an actively inflamed joint. Serum taken from an area of inflammation contains no uric acid, even though it be abundant in the blood from other parts of the body. The acid is either destroyed within, or is repelled from the region of inflammatory action.

By this method the presence of uric acid in the blood can be demonstrated in all cases of gout. It is usually more abundant during acute attacks of the disease, but it can be also discovered during the intervals of apparent health, as well as in cases of chronic and irregular manifestations of arthritism. Nor is it in the blood alone that the acid is present. It can be found in all the liquids and tissues of the body. It is demonstrable in the serous fluids, in the lymph, occasionally in the perspiration, in morbid exudations, and even in the serosity that moistens the surface of an eczematous patch.

An approximately quantitative estimate of the amount of uric acid in the serum was arrived at by Garrod, who found that crystals of the acid could hardly be rendered visible with the microscope unless they exceeded one part in sixty-five thousand; and in order to appear really numerous they must reach the proportion of one part in six or seven thousand parts of liquid.

The state of the red corpuscles of the blood is not always the same. Garrod and his successors found little change in their number, but in chronic forms of the disease the evident anæmia indicated a reduction in their number and in the amount of hæmoglobin. This impoverishment of the blood is not usually so great as it often appears to be in chronic rheumatism, unless the occurrence of gout is associated with lead poisoning. When that complication exists the severest forms of anæmia are developed, and there is great destruction of the red blood corpuscles, with corresponding debility and exhaustion of the patient. Comparatively little is known about the modifications of the blood-plasma. There is an increase of the fibrin-forming elements in acute cases of the disease, so that the blood drawn from such patients rapidly coagulates into the small and contracting clot that is characteristic of active inflammation. Unless renal disease should coexist, the albumin exhibits no change of any appreciable character. Even then the albuminous loss through the kidneys is too small to exert any notable effect upon the composition of the plasma. The same thing is probably true of the alkalinity of the blood—we are not in a position to estimate accurately its changes. The presence of oxalic acid in the blood was frequently noted by Garrod, but this should not occasion surprise, since oxalic acid may be obtained by splitting up the molecule of uric acid, and under cer-

tain circumstances one of these acids could not be present without the coexistence of the other.

Despite the fact that uric acid is usually overabundant in the blood of gouty subjects, there are cases on record in which the most careful analysis has failed to demonstrate its presence, even though the joints were thickly incrusted with tophi. *Per contra*, in cases of cirrhosis of the liver, gravel, and leukæmia the blood contains an excess of uric acid without any manifestation of gouty symptoms. According to Haig, those symptoms are developed not by the free circulation of uric acid in the blood current, but by its determination from the blood into the articular structures.

The Urine in Gout.

Much confusion exists in the writings of the earlier authors regarding the condition of the urine in gout, owing to faulty methods of analysis, and to the variable quantity and quality of the urine itself in the different stages of the disease. In order to arrive at accurate knowledge the daily quantity of urine should be ascertained for a period of several days or weeks; and the amount of uric acid should not be estimated from the daily sum total, but from each specimen that is voided at stated intervals during the twenty-four hours. This precaution is rendered necessary by the fact that the discharge of uric acid is not uniform, but is subject to great and rapid variations. During an acute attack of gout the urine exhibits the ordinary characteristics of febrile urine—it is scanty, high-colored, acid, often increased in specific gravity, yet containing little uric acid. After the attack, and during convalescence, the urine becomes abundant, of a lighter color, and richer in uric acid. The recent investigations of E. Pfeiffer (*Berliner klinische Wochenschrift*, 16, 17, 19, 20, and 22, 1892) agree in this particular with the earlier observations of Garrod. According to Pfeiffer, the secretion of uric acid is diminished in acute gout, while it is increased in the chronic forms of the disease accompanied by incrustation of the joints. He is also of the opinion that while the production of uric acid is not increased in acute gout, in the chronic stage it does show an increase. In both forms of the disease metabolism is diminished and the excretion of urea is also reduced accordingly. The analysis of Garrod showed that in acute gout, and in chronic gout with or without uratic deposits, there was a reduction of uric acid in the urine to a point below the normal physiological amount. These observations have been repeated and confirmed by a number of chemists.

On the contrary, however, Bouchard, Lécorché, and the later

analysts have reported an array of causes in which the quantity of uric acid, though somewhat diminished before an attack of acute gout, rises to the normal figure, or even exceeds it, during and after the attack, unless the kidneys had been injured by chronic inflammation. Haig has recently shown that these apparently contradictory statements can be reconciled by taking into account the fact that for every individual the average ratio between uric acid and urea in the urine remains about the same when a long period of time is taken into consideration. So that it becomes necessary to measure the quantity of urea as well as of uric acid that is voided, and to ascertain the quantitative relation between these two substances, in order to decide whether uric acid is really being voided in excess at any given time in the course of the disease. The normal proportion between uric acid and urea is about 1:35. Now, if this proportion be disturbed so that the urine contains the two substances in the ratio of, say, 1:28, it can be asserted that uric acid is voided in excess, even though the sum total of urate be less than in healthy urine. Since the formation of uric acid is assumed to take place at a rate that is uniform with that of urea, the quantity that is actually formed in the body may be indicated by the amount of urea that is excreted in the urine; consequently, the oscillation in the discharge of urates is due to retention and to subsequent reactionary excretion rather than to any considerable variation in production. Therefore, gouty patients (whose kidneys have not been ruined by chronic nephritis) if they consume large quantities of animal food, will excrete large amounts of urea and urates; but, if they become feeble and cachectic, the formation of nitrogenous excreta will sink below the normal level. And when from any cause a temporary retention of urates occurs, it will be followed by a sufficiently excessive discharge to even up the ratio.

In this way, it may be possible to reconcile some of the apparent disagreements of observation. When normal urine is rich in urea, it is acid, and the blood is also more highly charged with acid. The proportion of uric acid to urea may then fall to 1:35, or even less; there is apparently less uric acid in the urine and in the blood. But if the amount of urea be reduced, acidity of urine and blood will fall, and the urates will increase in both. Such oscillations are conditioned by the diet, and by the time of the day. During the daytime, the blood and urine are rendered less acid by the absorption of food from the alimentary canal, and they can therefore hold in solution and can transport a larger quantity of urates. During the fasting period of night, the conditions are reversed: the blood and urine become more acid and are less capable of carrying urates.

Now when by the agency of disease a similar modification of the urine is effected, the quantity of urates that are voided is correspondingly modified. During an attack the highly concentrated acid urine receives a smaller excretion of urates because the over-acidulated blood cannot transport them (Garrod). They are retained in the tissues, and remain there until the subsequent reaction occurs, when the now abundant, limpid, and alkaline urine receives from the less acidified blood the excess of urates that have been retained in the body during the febrile paroxysm. But if the patient has been a vigorous and voracious feeder till the time of the attack, his urea and uric acid may be so abundant as to prevent the reduction of nitrogenous excreta that would have been otherwise apparent. With returning health, he resumes his faulty habits, and very little, if any, reduction can be noted at any time (Bouchard).

The quantity of urea that is voided with the urine does not exhibit any special variation that cannot be explained by the change of diet in an acute attack of gout. Heavy feeders, who indulge in animal food till the outset of the attack, show little reduction of urea until fever and loss of appetite cause abstinence from the nitrogenous elements of food. In like manner, the degree of appetite and of indulgence during chronic gout determines the quantity of urea. Hearty eaters void the full amount, while cachectic patients and vegetarians yield only a comparatively small quantity.

The phosphates exhibit less agreement with the character of the diet, because they are so largely the result of metabolism within the tissues. For this reason, the quantity will vary according to the rate of disassimilation. In young and vigorous patients the discharge of phosphates may be actually increased during an attack; but with old, atonic, and cachectic subjects, there will be a reduction below the normal figure. Much also depends upon the state of the kidneys in the determination of this matter.

A highly acid state of the urine forms a common characteristic of arthritic subjects. During the state of comparative health that precedes or follows an attack, the persistent acidity of the urine is a notable fact. This is due to the presence of the acid phosphate of sodium, a salt which, if it should exist in the blood, would interfere with the solution and excretion of urates. On the contrary, the disodic hydrogen phosphate (Na_2HPO_4) which is the normal sodium phosphate of healthy blood, is an excellent solvent of urates, hence the advantage of a highly alkaline state of the circulating fluids, enabling them to transport and to discharge in a soluble state the uric-acid salts with which they come in contact. Sir W. Roberts has shown (*Lancet*, June 18th, 1892) that these salts normally exist in the

fluids of the healthy body in the form of quadri-urates, which are easily soluble and are readily passed through the kidneys. But, in the uratic deposits which infiltrate the joints and other structures of the gouty, the urates are present as bi-urates, the most stable and insoluble salts that are formed with uric acid. In the ready transformation of quadri-urates into bi-urates, and *vice versa*, lies, according to Roberts, the explanation of many of the phenomena of gout. The uratic sediments that are so frequently precipitated from the urine as it cools, consist of quadri-urates which are soluble at the temperature of the body. The crystals of uric acid, like grains of red pepper, that are deposited from highly acid urines, are liberated by the decomposition of quadri-urates that have been held in solution at the normal temperature. These quadri-urates are very unstable, and, after their precipitation from the urine as it cools, they break up into uric acid and bi-urates. Contaminated with urinary pigment, the bi-urates constitute the brick-dust sediment that is redissolved when the urine is again heated. The liberated uric acid rapidly crystallizes in various modifications of the rhombohedral form, and sometimes exhibits a considerable deposit that is readily distinguished with the microscope from the amorphous bi-urates that form the bulk of the precipitate. According to Roberts (*Lancet*, June 25th, 1892), this process does not essentially differ from the gradual liberation of uric acid that takes place slowly in all healthy urine which has been guarded against fermentation. Acted upon by the water of the urine the quadri-urates slowly break up into bi-urates and free uric acid. The bi-urate is immediately retransformed by double decomposition with acid sodium phosphate into a quadri-urate, which is again broken up by the action of water; and thus the process goes on until all the uric acid has been set free. The presence of pigment, for which urates manifest a strong affinity, seems to exert a retarding influence upon these chemical reactions; otherwise, there is no apparent reason why uric acid should not be always precipitated within the urinary passages. The failure of such inhibition is probably one of the most powerful causes of the deposit of uric acid and gravel that actually takes place in the renal pelves and in the bladder, in certain forms of arthritism. "The conditions of the urine which tend to accelerate the precipitation of uric acid are high acidity, poverty in salines, low pigmentation, and high percentage of uric acid. And, conversely, the conditions that tend to postpone precipitation are depressed acidity, richness in salines, richness in pigments, and low percentage of uric acid—probably the most important of these factors is the grade of acidity" (Roberts, *Lancet*, June 25, 1892, p. 1,401). It is highly probable that whenever simi-

lar conditions obtain in the blood and lymph, a similar reaction on the part of uric acid may occur in those fluids or in the tissues that they irrigate. In the pathological establishment of such conditions consists the initial process of gout.

Symptomatology of Gout.

Before passing to the consideration of the symptoms of an acute attack of articular gout, it is important to know its antecedents; in a word, to recognize the signs that characterize the arthritic diathesis.

By this term is meant a predisposition to a certain class of disorders and diseases that are naturally related to each other. The predisposition is usually inherited, but it may be also acquired. The signs of a diathetic tendency are not always well marked, but in many instances their array is complete, and as conclusive as an articular attack itself could be. Often, however, only one or two marks of the tendency are apparent, and, especially among children, the scattered evidences need the support of a definite family history in order to render them instructive. They should never be overlooked, for in many doubtful cases they may furnish the clue to a most suggestive and fruitful line of inquiry.

One cannot be too often reminded of the fact that the existence of a diathetic predisposition is incompatible with perfect well-being. The individual may appear to be in the enjoyment of blooming health; his color is high, his flesh is firm and abundant, he is continually in the receipt of congratulations upon his vigor of mind and body. Despite all this, a careful physical examination will never fail to reveal some departure from the normal standard long before the outbreak of an acute attack of the disease. In many instances, where the habits of life and the diet preclude all possibility of articular inflammation, the evidences of abarticular or irregular gout may be discoverable. It is thus that among children the proof of arthritism may be often gathered from the concurrence of a suspicious family history and certain skin diseases that are not in themselves specially significant. Unless guided by a characteristic family history, it is often difficult to decide whether certain unhealthy manifestations in infancy should classify the patient as arthritic or scrofulous.

Among the earliest manifestations of infantile arthritism is the frequent occurrence of indigestion. The child may be fat and hearty, blessed with the best of appetites, yet subject to colic and constipation, or looseness of the bowels. The face and scalp are disfigured by an obstinate and intensely painful eczema. The eruption may be either dry or moist, and it itches frightfully, so that the hands have

to be tied in order to prevent scratching. Yet there is nothing pathognomonic about this eruption. It is its obstinacy, its concurrence with other arthritic disorders, and a bad family history that serve to classify it among the precursory phenomena of arthritism.

We are not yet in a position to distinguish infallibly between the two great diatheses, the arthritic and the scrofulous.

Besides eczema, the teething infant is prone to other itching eruptions. Urticaria, erythema, lichen, and various unclassifiable pruriginous irritations of the skin may occur without any apparent cause. They seem to be dependent upon an excessive sensitiveness of the cutaneous tissues that permits them to experience morbid excitement from causes that are insufficient to arouse the corresponding structures in a healthy body.

In like manner the mucous surfaces of the internal passages exhibit similar irritability. The slightest exposure to a draught or damp air causes the patient to "take cold." Coryza, pharyngeal catarrh, laryngitis, laryngismus stridulus, bronchitis may follow each other in quick succession or may concur with alarming facility. But these inflammations are usually of short duration, and do not display the persistent tendency to tedious muco-purulent discharge that characterizes similar affections in a scrofulous child. Inspection of the throat more frequently reveals a chronic granular pharyngitis rather than the indolent tonsillar hypertrophy that belongs to scrofula.

Another manifestation of the gouty predisposition is sometimes witnessed in the form of headache. This assumes the form of periodical and recurrent headache—usually described as hemicrania or migraine. It is usually encountered among the children of parents one or both of whom have suffered with the same malady. In one instance that came under my observation the record of migraine could be traced back, over a line of gouty ancestors, for a period of four hundred years. Cases are not uncommon among children of six or seven years—sometimes as early as three,—giving occasion at this early age for anxiety regarding the possibility of tubercular meningitis as the exciting cause of the headache and vomiting that are so violent and exhausting. In many instances these recurrent headaches form the only conspicuous evidence of arthritism during early and middle life, if the habits of the patient do not provoke the characteristic articular lesions.

With the approach of adolescence, it is not an uncommon event to experience bleeding from the nose—occasionally at the time of headache, or without evident provocation. Such hemorrhages are analogous to the hemorrhoidal fluxes and the paroxysmal hæmoglobinurias of later life.

At the age of puberty attacks of articular inflammation that cannot be distinguished from acute rheumatism are not unusual. Purpura sometimes occurs, either with or without the usual visceral or articular disturbances that accompany non-arthritic forms of the disease. It is at this period of life that the tendency to cutaneous disorders which marked the years of infancy again appears, to embitter the experience of the adolescent patient. Obstinate eczema once more attacks the folds of skin in the flexures of the larger joints, and about the smaller articulations of the hands and feet; often exhibiting a notable tendency to symmetrical eruption upon the two halves of the body. Acne begins its tedious course upon the temples, nose, cheeks, and shoulders. Sometimes successive attacks of boils appear upon the neck and back. The pustules of acne are frequently of an almost furuncular character, with indurated bases and an indolent course that is marked by passive congestion and a violaceous hue. These patients usually have an acid stomach, constipated bowels, and a tendency to hemorrhoids or to pruritus ani, especially in connection with the hepatic congestions that are determined by the changeable weather during the spring and autumn of the year.

The pharyngeal mucous membrane at this age exhibits, in a more pronounced form than in early childhood, the granular appearance that is caused by chronic inflammation of its follicles and other mucous glands. A spasmodic tendency is evident in connection with the bronchial inflammation that occurs. The patient wheezes and coughs with such violence as to suggest the onset of asthma. Hay asthma sometimes occurs during the summer months.

The organs of generation give evidence of participation in the universal over-sensitiveness that is so prominent a feature of the arthritic diathesis. The menstrual flux is irregular in its occurrence, and the young woman suffers with delay in the establishment of the flow; it may be either excessive or scanty, or it may be attended with severe lumbo-sacral pain. Headache is also a common incident, either before or after the monthly period; and it assumes the usual characteristics of hemicrania.

The intellectual faculties sometimes share in the disturbance at this time; the patient is irritable, peevish, and depressed. Young men display a similar exaggeration of the emotions in association with an inordinate irritability that takes the form of prolonged and uncomfortable erections, with nocturnal emissions. Herpetic eruptions sometimes appear upon the glans and prepuce. The urethra is readily inflamed, so that infection produces most painful and persistent forms of gonorrhœa. Even without infection, attacks of urethritis sometimes exhibit a degree of severity that completely rivals the

genuine venereal disease. Such forms of urethritis are liable to frequent relapses, and they often subside into a chronic gleet that is almost incurable. This state of things is usually accompanied by an over-acid state of the urine which is probably one of the principal causes of the persistence of the inflammation. In arthritic children and adolescents, the act of micturition is frequently attended by severe cutting pain along the urethra, even when no inflammation is present. This is due to the action of acid urine upon an inordinately sensitive mucous membrane. So hyperæsthetic are certain individuals that a few glasses of beer, champagne, or cider may suffice to determine a urethral crisis, especially if accompanied by venereal excitement of any sort. The urine, in such cases, frequently deposits a sediment of urates or of uric acid, on cooling. This, however, should not be deemed a symptom of importance, unless associated with other evidences of the arthritic diathesis, or unless the incident is often repeated.

During the period of adolescence, headache is frequently experienced. Any little disorder of the digestive organs is apt to be accompanied by an attack of migraine; and in many instances it recurs without any apparent cause. Sometimes it assumes the character of a dull, ill-defined feeling of weight and pressure within the cranium, rendering the patient temporarily incapable of mental application. Sometimes the pain assumes a more distinctly neuralgic character. The eye may become intensely painful, though exhibiting no evidence of other disorder. Often the sufferer experiences violent shocks of shooting pain that dart like a flash from one part of the head to another, constituting a local manifestation of a general tendency to lancinating pains in other organs and parts of the body—quite like what is so frequently experienced in tabes dorsalis.

Digestive disorders, which were usually brief and transient in childhood, now become more serious than formerly. The arthritic subject usually enjoys a good appetite, and is liable to overload his stomach. Fermentation, acid eructations, and accumulation of gas in the alimentary canal, now occur. The stomach becomes distended —it may finally be dilated—and there is a constant feeling of uneasiness in the epigastric region. The act of eating usually adds to the distress, and may be followed by painful irradiations into the hypochondria and interscapular space. The appetite may be extinguished, or it may exhibit great exaggeration and perversion. Young women manifest a craving for all sorts of indigestible and inedible articles. Often there is a longing for acids, pickles, spices, and their like. Sometimes, especially when the stomach is empty, there is great abdominal pain, accompanied by feelings of intense exhaustion.

This variety of pain differs from that of colic or ordinary neuralgia, and is probably seated in the sympathetic visceral plexuses. So general does the disturbance become, that distant organs may be involved in the paroxysm of distress. The association of headache with gastralgia, nausea, and vomiting has been already noted. The heart also shares in the disorder—exhibiting disturbances of the rhythm and force of its beat. Violent palpitation, irregular and intermittent pulsation, with temporary dilatation of its cavities, and feeble circulation of the blood in the extremities and organs of the body, are common consequences of the irritable weakness that is thus rendered apparent. Sometimes an attack of vertigo adds to the confusion and distress of the sufferer, though this complication is unusual before the latter half of life is reached.

In many instances dyspepsia seems to be of gastric origin, but in many others the liver appears to be the principal seat of disorder. There is a bitter taste in the mouth, especially on rising in the morning. A yellow fur befouls the tongue; the mouth is sticky, and the breath may become offensive; the bowels are sluggish; the urine is high-colored and loaded with pigment; the skin becomes slightly jaundiced. This array of symptoms may persist for a long period of time, and may disappear by gradual resolution. But it may become aggravated, and be finally accompanied by evident enlargement and tenderness of the liver. A sensation of weight and dragging pain may be experienced in the right hypochondrium. At last the difficulty culminates in a "bilious attack" characterized by headache, bilious vomiting, and sometimes by brief diarrhœa, after which the patient feels greatly relieved. In certain cases, however, the phenomena of intestinal dyspepsia become quite confirmed. The stomach may not be involved, and in such case there is no dyspeptic disorder until an hour or two after eating. Then the abdomen feels tense and uneasy; there is great flatulence, and gas escapes in considerable quantity from the anus or lingers in the coils of the intestines, where it intensifies the discomfort of the sufferer. The fæces are usually clay-colored, often scanty and constipated, or passing off after the fashion of a mild diarrhœa. But in many instances the disorder is only terminated when its symptoms are merged in a full-blown attack of articular gout. Sometimes it is possible for an experienced patient thus to be forewarned of an approaching attack by the clay-colored stools and the general disturbance of intestinal digestion, indicative of retention of biliary excreta as well as of delay in the discharge of urates through the kidneys. After the crisis of an attack there is usually an excess of all these substances in the fæces and in the urine, indicating a close connection between their retention and the phe-

nomena of the disease. Thus it appears that the dyspepsia with which these patients suffer, though usually involving the stomach and all below it at the same time, may sometimes attack the stomach alone or the liver and its dependencies alone. The victims of hepatic dyspepsia lose their appetite, and instinctively crave acids, spices, bitters, coffee, and alcoholic stimulants, to aid in its recovery, though such artificial provocatives usually do more harm than good. They also tolerate animal food that is deprived of fat; but they cannot easily digest sugars, starches, or farinaceous articles of diet.

Among the other premonitory symptoms of gout have been noticed a tendency to subconjunctival congestion affecting the sclerotic and the conjunctiva in the neighborhood of the insertion of the ocular muscles. It is usually a transient phenomenon, and is sometimes noted among rheumatic subjects. Scintillant scotomata and hemianopsia are also sometimes experienced in the form of brief paroxysms of the disorder. Grinding of the teeth during sleep occasionally happens at any age, but it is more frequent among patients in later life. Sometimes their molars are worn nearly to the gums by this mode of attrition.

The depression of spirits that has been already noted sometimes, especially among elderly patients, reaches the level of hypochondria, or even of melancholia. The whole character is temporarily altered; the busy leader of men becomes incapable of restraining his own temper, or of caring for anything but the incidents of his own wretched health. He is irascible, unreasonable, and sometimes violent in his behavior. Witness the lives of Frederick the Great and his father. Of the hypochondriacal condition, the famous Lord Chatham exhibited during his later years a most illustrious example, graphically narrated by the historian Lecky ("History of England during the Eighteenth Century," Vol. III., pp. 133–156). In certain cases, probably predisposed to mental derangement, such periods of wretchedness always precede an attack of gout, and are as invariably dissipated by the outbreak of inflammatory symptoms.

The phenomena of lithiasis, of the hepatic variety as well as the renal, are not uncommon precursors of a gouty attack. They occur after the usual fashion of biliary colics, accompanied by pain in the stomach, vomiting, and jaundice. Or there may be excruciating pain along the ureter, radiating down the spermatic cord, and associated with retraction of the testicle, high-colored or bloody urine, and finally the discharge of a calculus or a quantity of renal sand.

Sometimes the respiratory organs are the chief seat of disturbance. Violent fits of sneezing, followed by a copious watery discharge from the eyes and nasal mucous membranes, may occur in

paroxysms of short duration, counterfeiting, while they last, the symptoms of hay fever. In other cases the bronchial mucous membrane bears the brunt of the attack, and for several hours at a time the patient displays the characteristic phenomena of spasmodic asthma. Occasionally, the œsophagus is involved in a spasm of brief duration, attended by difficult and somewhat painful deglutition and a general sense of suffocation. Gastralgic paroxysms are not infrequent, during which the sense of constriction at the base of the thorax and the obstinate vomiting and pain are not to be distinguished from the agonizing "gastric crises" of tabes dorsalis. Such attacks are more frequent in the third decade of life than at an earlier age.

It might be anticipated that with such an enormous list of premonitory disorders the general health of an arthritic subject must suffer severely. On the contrary, however, the individual usually retains the appearance of vigorous health. The patients are few who present at the same time any considerable number of the above-mentioned disturbances of function. Sometimes it is true that in the same person are united many of the phenomena that are characteristic of the arthritic diathesis; but in numerous cases it is necessary to seek in the family history and habits of the individual an explanation of the rare and trifling disorders that precede and advertise the advent of an attack of gout. The future patient is fat and fresh looking, frequently athletic and muscular. During the third decade of life the hair frequently begins to whiten and to fall; though in many instances it remains luxuriantly abundant to the last. Dandruff often appears upon the scalp, on the chin, and occasionally among the pectoral hairs upon the sternal surface of the thorax. The pustulation of acne often deforms the adolescent visage, and a suspicion of eczema may be sometimes detected in the furrow behind the ear or at the base of the ala nasi. Perspiration flows at the slightest provocation, and there is an uncomfortable sensitiveness to draughts of chilly air. In the folds of skin under the breasts, in the groins, and around the arms, intertrigo is not uncommon. Urticaria frequently appears, and herpetic eruptions break out upon the prepuce and glans; varicocele, hemorrhoids, and varicose veins become annoyingly prominent, and are frequently associated with acid dyspepsia, constipation, headache, and vertigo. The urine is either copious and charged with urates, or it may be scanty, high-colored, and acid. From time to time the respiration is disturbed by an attack of spasmodic breathing, and the heart is often palpitating, irregular, and feeble in its action. Sometimes, instead of a fair complexion, blond hair, and corpulent figure, the patient presents the characteristics of

the bilious temperament, harsh features, a dark complexion, and an angular frame. In such cases constipation, hemorrhoids, bilious derangement, and melancholia have been thought to be more conspicuous than among those of a florid type; but it is probable that the predominance of certain symptoms is controlled by the diet, habits, and conditions of life as much as by the original constitution of the body. Thus it is a matter of common remark that dyspeptic symptoms are most conspicuous in the arthritic rich who overfeed themselves and lie in the lap of luxury. They suffer with congestive headaches, epistaxis, or bleeding piles; seem very ill for a short time, and then quickly recover their ordinary vigorous health, which persists until the next paroxym, or until the precursory ailments are replaced by an attack of genuine gout. Among the nervous and ill-nourished subjects of arthritism, headache, insomnia, and neuralgia are the frequent signs of the diathesis. Their dyspepsia is of the nervous variety—it is less severe, but more persistent than the corresponding form of indigestion that exists among vigorous and robust individuals. They suffer with functional disturbances of the heart, and with bronchitis that is often accompanied by spasmodic disorders of respiration. When, at last, the acute attack of gout is developed, it is not so sudden, or so violent, or so brief as when it appears in a plethoric subject. Its course, also, is usually more prolonged; recovery is less rapid and perfect; and there is greater danger of the establishment of permanent disability. The whole course of events is controlled by the original constitution and temperament of the patient. The most notable symptoms are furnished by the weakest organs of the body, and consist chiefly in an exaggeration of functional defects which in ordinary health are present but not obtrusive.

From this array of phenomena it is evident that the precursory symptoms of gout may involve a disturbance of every organ and function of the body. Long before the final explosion, the arthritic subject has had much experience of ill-health. The paroxysmal character of these episodes, their brevity, and the temporary relief that they afford, serve to indicate their kinship to the real articular attack of gout. It is their existence and their persistent recurrence that indicate the arthritic diathesis, even though, by reason of wholesome living, they may never culminate in the acute disease. Recognition of their presence and significance is of the highest importance, since upon such early and intelligent diagnosis is based the whole art of prophylaxis and of physical education during the early years of life.

Symptoms of Acute Gout.

The onset of an attack occurs in no uniform fashion. Sometimes it comes on suddenly, in the midst of perfect health, and the patient is waked in the middle of the night by a terrific pain in the foot. Sometimes, after the occurrence of various premonitory symptoms, as above described, all pain and uneasiness cease; there is perfect relief from suffering; the spirits rise and become buoyant; an exaltation of function is evident in every organ of the body. But this is only a deceitful lull in the storm, and after a few hours of comfort, the attack is ushered in as usual with an agonizing nocturnal paroxysm. With certain patients this mode of attack is uniformly experienced with every recurrence of the disease. In other instances, however, the premonitory symptoms persist for a long time, and increase in severity until the very moment of the articular paroxysm.

In many cases the future localization of the disease is predicted by antecedent pains of a rheumatic character that hover around the joints, especially in the lower extremities. Sometimes they are associated with slight articular swelling that suggests the imminence of an attack of rheumatism. Still more emphatic is the appearance of turgescent veins in the leg, premonitory of the swollen veins that are to be found in the neighborhood of an acutely inflamed gouty joint. Among certain patients, the attack is immediately preceded by a feeling of profound prostration and universal exhaustion. This experience is often a consequence of some form of physical or mental over-exertion. Thus, it may follow excessive fatigue after a long walk, a debauch, a venereal extravagance, or an intellectual effort of unusual duration and intensity. The patient seeks his couch in a condition of feverish lassitude very similar to that of influenza, and before morning the great toe is violently inflamed.

But, however advertised and foreshadowed, the acute attack is marked by a paroxysm of painful inflammation that has no parallel in other diseases. It is usually in the middle of the night, between the hours of twelve and two, that the patient is waked by a horrible pain in the arch of his foot, or at the base of the great toe. He moves and twists and turns; he draws up his leg, and then pushes it out again; he tries every possible change of position; but in vain. The pain will not cease. At first, it seems like that of a sprain or a bruise, and the mind calls up all the incidents of the preceding day in search of some accidental cause for such distress. As the hours roll on, the agony increases; it is a biting, tearing, crushing pain, as if the member were being rent by the teeth of a tiger, or were

slowly yielding to the compression of a vise. The sufferings are increased by recurrent spasmodic muscular contractions that shake the limb. The weight of the bed-clothes is intolerable, and every movement of the bed itself is unendurable. Besides pain there are redness, heat, and swelling in the affected part. A universal fever burns the patient; all the classical symptoms of acute inflammation are present.

Fortunately, however, the paroxysm is not interminable. Toward three or four o'clock in the morning a gradual subsidence of the pain begins. Slowly the fever yields; a gentle moisture bedews the forehead; sleep comes at last, and with it some degree of imperfect repose. When, at a late hour of the morning, the patient awakes, his foot is lame and tender, and the great-toe joint is swelled and red. Still, the day may be passed in comparative comfort; but as evening returns the paroxysm is renewed, though usually with a degree of severity that does not quite equal that of the previous night. It reaches its height soon after midnight, and then subsides again at the approach of morning. In this way with gradually decreasing intensity the successive paroxysms follow each other for several days —perhaps for an entire week. Little by little the swelling disappears; fever ceases its manifestations; appetite returns; and in a few days the patient is restored to his usual health.

Briefly stated, such is the course of typical, acute articular gout, involving the metatarsal joint of the great toe. Reviewing the individual symptoms, it is evident that pain is the first and most conspicuous phenomenon. It ushers in the attack, and is intolerable before the appearance of redness and swelling. It is felt not so much in the joint between the bones, as in the phalanges themselves—especially upon the lateral borders. In many respects it resembles the throbbing, lancinating pain of a whitlow. It differs from the pain of acute rheumatism by its continuity and its independence of movement and pressure, whereas pain at the beginning of a rheumatic attack is aggravated by motion and flexure of the joint. Sometimes, even among vigorous subjects, the suffering is quite endurable; but usually words fail to indicate the agony of the patient. In certain cases the feeling is like that of a dislocation; in others the toe aches as if it had been long immersed in ice-water, or there are sensations as if melted lead or boiling oil were trickling down the calf of the leg. These are subjective sensations which are not provoked by any form of contact with the limb. If the joint be touched or rubbed or moved, the only feeling excited is that of intense pain that radiates from the joint through the entire member. The perceptions of heat, cold, and contact are all merged into one common distress.

Swelling is another of the conspicuous phenomena of the attack. Even before its invasion, the superficial veins of the limb become enlarged, and with the outbreak of the paroxysm the joint which is its seat is surrounded by a network of turgid and somewhat varicose vessels. The skin assumes a purple hue, and grows rapidly œdematous. The cavity of the joint, the neighboring bursæ and tendinous sheaths are also filled with a serous exudation which adds to the swelling and tension of the part. Even the periosteum in the vicinity of the articulation shares in the universal infiltration. From the toe the swelling extends, in the severest cases, over the upper surface of the foot, sometimes as far as the ankle itself. This is especially true of cases in which the sheaths of the large tendons are involved: the œdema occupies the dorsal and the plantar regions, and sometimes is so great as to cause a sort of fictitious fluctuation along the line of the metatarso-phalangeal articulations. But, ordinarily, the swelling is restricted to the immediate territory of the affected joint.

Pain and swelling are always associated in gouty inflammation, but their incidence is not always simultaneous. Sometimes the joint begins to enlarge before it is painful; in other instances pain is experienced for a considerable time before the appearance of swelling. In this respect, the parallel with rheumatism is very close. In certain cases there is considerable reduction of suffering as soon as the joint begins to swell.

Another prominent characteristic of acute gout consists in the redness of the affected joint. The integument is of a dark red or purple color that is much more pronounced than the coloration of rheumatic swelling. In severe cases of rheumatism there is a rather insignificant injection of the skin about the joint and over the sheaths of the large tendons; usually, there is very little change of hue upon the swollen surfaces. But in acute gout the swelling appears tense, and the skin is red and shining, as if an abscess were about to break through its surface. Pressure causes the bright color to disappear for a moment, but it immediately returns as soon as the finger is removed, and with it comes an aggravation of pain. Quite often the formation of an abscess is still further counterfeited by a deeper redness and greater degree of swelling upon the lateral surfaces of the great toe. The extent of cutaneous discoloration is conterminous with the swelling in severe cases, and its intensity corresponds with the severity of the attack. But in old chronic cases there is usually very little color, though there may be great and persistent œdema.

Unlike the onset of pain, the color of the inflamed part does not reach its maximum at the beginning of the attack. It first shows itself at the crisis of the initial paroxysm, and only reaches its great-

est brilliancy during the second night. After the first twenty-four hours the bright tints are transformed into a violet purple hue, which gradually fades as the nocturnal paroxysms diminish in severity.

The temperature of the inflamed point rises from two to four or five degrees Fahr. during the attack. Thus it is evident that all the classical symptoms of genuine inflammation are exhibited in the affected part. Another evidence of local cutaneous inflammation is afforded by the exfoliation of the cuticle that follows the subsidence of acute symptoms. The scarf-skin peels off in flakes, and the process, which is accompanied by considerable itching, is sometimes prolonged for more than a week.

The fever that prevails during the attack does not always correspond with the local symptoms. The pulse often fails to reach one hundred beats in a minute, and the fever-heat seldom rises so high as 102° or 103° F. Excessive temperature and a rapid pulse are the exception rather than the rule. Probably the most constant of the febrile symptoms is the gastric disorder that is associated with the attack. The breath is very offensive; the tongue is large and flabby, and is covered with a thick yellowish coat; there is an utter disgust for food, but thirst is intense; there is a bitter taste in the mouth; acid eructations and hiccough are very commonly experienced. Vomiting seldom occurs, but the bowels are constipated. There is considerable tenderness on pressure over the epigastrium, and the liver is somewhat prominent below the ribs, unless pushed upward by intestinal flatus.

During the acute paroxysm the urine presents the ordinary characteristics of febrile urine; it is scanty, high-colored, but does not contain bile-pigment. Usually it contains urates and uric acid in considerable quantity, though the amount is generally less than is discharged during the intermissions. Sometimes, when the attack is severe, there may be a trace of albumin in the urine, but this is a transient febrile phenomenon, and it disappears in the course of a few days without damage to the kidneys. As the attacks decline, the secretion of urine becomes more profuse, and sometimes assumes for a few days the character of a veritable polyuria.

Convalescence in the case of a young and vigorous subject, especially after a first attack, is usually rapid and leads to perfect recovery. The inflamed joints exhibit their original flexibility, without any trace of swelling or other impediment to motion. In many instances the general health is greatly improved, and various ailments that have been mentioned among the forerunners of an attack of gout are now completely relieved.

But, on the other hand, there are patients who are less fortunate.

Œdema sometimes persists for a long period after the disappearance of other inflammatory symptoms. In other cases, though there be no swelling nor mineral deposit, the joint remains stiffened, and inordinately sensitive to changes of temperature. Many individuals even after a brief attack are greatly debilitated, as if they had been ill for weeks or months. Sometimes there is considerable emaciation, and the muscles on the proximal side of the affected joint may undergo atrophy, just as they may dwindle after a severe attack of rheumatism, or after a traumatic inflammation of a joint. In a certain number of cases, the attack degenerates into chronic gout; the joints remain permanently enlarged, and a uratic deposit rapidly makes its appearance in the peri-articular tissues.

The tendency to localization in the great toe is one of the most notable facts in connection with the first attack of acute gout. Garrod was of the opinion that not more than five per cent. of cases escaped without an initial inflammation of the joints of the great toe. Of forty cases reported by Braun, there were only two in which the inflammation did not begin in the toe or in the metatarsal region. Scudamore collected a total of five hundred and sixteen cases, in which the joint of the great toe was attacked in three hundred and seventy-three instances, while both toes were simultaneously inflamed in twenty-seven cases. Occasionally, however, any one or all of the principal joints may be involved, while the great toe escapes entirely. In such cases, however, it is sometimes possible to identify a cause for such an irregular localization: the occurrence of a previous injury, a sprain, a bruise, an unusual degree of exercise in walking, may determine the outbreak of inflammation in the ankle, the knee, the wrist, or the elbow. Thus, an elderly prelate of my acquaintance, finding himself at an out-of-the-way station in the country, without means of conveyance, was obliged to walk for several miles to the church where he was to officiate. An attack of gout in the knee-joints followed this unusual exertion. In this respect, the manifestation of gout sometimes follows the same course that has been often observed in the localization of articular rheumatism and of syphilis. Occasionally, after a general shock or injury, such as may be produced by a fall or a concussion, the localization of an attack of gout is widely diffused, and many of the joints are simultaneously inflamed. In such cases it may be very difficult to distinguish the case from an attack of rheumatism, but in the majority of instances it will be found, on careful inquiry, that the patient had suffered with one or more previous attacks in which the great toe alone, or in association with other joints, had been involved.

The manner in which an attack of gout is localized upon one or

upon several joints is not without importance in its relation to the prognosis. When one articulation alone is attacked, and when the severity of the paroxysms is great and sharply defined, the course of the disease is much more rapid, and recovery is more complete than when several joints are tardily involved. The intensity of the suffering that is experienced varies much according to the temperament of the individual. Nervous and excitable patients suffer more than those who are dull and phlegmatic. Recurrent attacks also serve to reduce the power of reaction, so that with return of the disease the onset is less acute, and the pain is less severe. But, even among the victims of chronic gout, it is not unusual to witness the occasional recurrence of an acute attack that is marked by a considerable portion of the vivacity of the original paroxysms.

Symptoms of Chronic Gout.

The progressively invasive character of gout has been already indicated. In typical cases of the uncomplicated disease, its first onset is experienced during the early years of the fourth decade of life. Either with or without characteristic prodromes, it breaks out suddenly with a violent nocturnal paroxysm that is repeated every night with declining severity for five or six times in succession, and at the end of ten days recovery is complete. Good health may be then enjoyed for many months, perhaps for a number of years. But a tendency to recurrence is usually evident; the attacks are repeated with the return of spring and autumn; they become less severe, longer in duration, and more frequently renewed. Instead of being restricted to the great toe, the œdema involves the arch of the foot, and persists long after the subsidence of inflammation. Both feet become involved, and all their joints are invaded by the progress of the malady. Then the ankles and the knees are attacked, and sometimes the fingers, wrists, elbows, and even the spinal articulations are infiltrated and inflamed. It is unusual to find more than two or three joints at once in a state of active inflammation; but the course of the disease is steadily progressive, advancing from the smaller joints to the larger, returning often upon itself, as if unwilling to quit the scene of initial disorder, but in the long run invading an ever-widening territory, and approaching the internal organs and important viscera of the body. Especially after middle life is it apparent that every exacerbation of the disease leaves the patient weaker and less capable of withstanding its inroads; he has become the victim of chronic gout.

Such is the usual course of evolution by which acute and sthenic

gout passes insensibly into the chronic form of the disease. But in many instances, especially among old people and among the descendants of a gouty ancestry, the acute stages of the disease are not manifested, and from the first it exhibits the subacute and lingering processes that are characteristic of its chronic form. A considerable number of elderly people find their joints gradually stiffened and hampered by the accumulation of urates in the articular tissues, without ever having experienced any of the painful inflammatory symptoms above described. Women after the menopause, and the debilitated scions of gouty families are not infrequently victims of this insidious variety of gouty arthritis, rendering evident the fact that the clinical forms of the disease are dependent upon the constitutional characteristics of the individual rather than upon the intrinsic nature of the malady itself. Keeping in mind this peculiarity, it will be impossible to fall into the error of supposing that mere duration of time and frequent recurrence of the attacks are sufficient to confer upon the disease the character of chronicity. Many an athletic subject has reached a vigorous old age without a single experience of chronic gout, though he may have had numerous acute attacks periodically recurring during the course of a long lifetime.

Two principal factors combine to constitute what is correctly termed chronic gout: the existence of a profound cachexia, and the establishment of permanent disability through infiltration of the joints and peri-articular structures with uratic salts. In acute gout recovery after an attack is perfect; the affected joints are soon capable of their ordinary movements, and the general health is often better than ever. But when the disease is chronic, there is no such elastic rebound; after every exacerbation the patient is left enfeebled, exhausted in mind and body, and more than ever predisposed to morbid function of his locomotive and nutritive organs. Despite the comparatively trifling severity of the active crises, they are more persistent and more injurious than the acutely painful attacks. Œdema becomes more extensive, and its duration increases until it finally assumes a permanent character. There is loss of appetite, continuous indigestion, intellectual torpor, and an increasing somnolence. With the progressive destruction of the articulations of the lower extremities the patient loses the power of walking, and exercise grows more difficult. This enforced confinement reacts prejudicially upon digestion, and a vicious circle is soon established, to the utter ruin of the health. Visceral complications supervene; the kidneys and the organs of circulation give way; and death results from toxæmia and exhaustion.

In the study of chronic gout it is, therefore, necessary to regard

particularly the two principal elements of the disease. They may be, in many instances, most intimately associated; but in many other cases they may be quite loosely connected. In the majority of patients who possess a vigorous constitution, the transformation of acute gout into the chronic malady is marked by a predominance of articular phenomena. The joints become extensively infiltrated and disorganized without any great deterioration of the general health. But in a considerable number of patients, especially among those who have inherited the arthritic diathesis, there may be extensive visceral disease and continuous ill-health without any very notable destruction or deformity of the articular structures. Among the older authors this variety was known as atonic or asthenic gout.

Passing now to a consideration of that variety of chronic gout in which the articular changes form the most prominent features of the disease, it is to be observed that a periodical recrudescence of the symptoms is still apparent. The attacks are recurrent, but they are less violent than formerly. There is less pain, though it is more continuous, and the limb can be handled and moved in a way that once would have been impossible. Swelling is not so narrowly circumscribed about a particular joint, but is rather widely diffused over the whole extremity. Redness does not appear; the swollen limb is white, and it pits on pressure; there is no cutaneous inflammation, consequently no subsequent exfoliation of the cuticle. But, with all this superficial show of moderation, the infiltration of the joints progresses at a rate that was unknown in the acute disease. The swelling of the joints persists for weeks or months after each attack, and consequently the articular capsule becomes dilated, and the ligaments are relaxed; the fluid contents of the synovial membranous sac are thickened with uratic crystals which accumulate in quantity sufficient to hinder the movement of the joint. At the same time the diarthrodial cartilages receive a deposit of urates in their subserous substance, after the manner that has been already described. As this process advances the motion of the joint is restricted in proportion to the degree of infiltration, and the fingers instinctively place themselves in the positions that create the largest capacity in the articular cavities. Since the position of partial flexion is most favorable to this end, the phalanges assume various degrees of semi-flexion or of alternate flexion and extension like what is often remarked in chronic rheumatism. In fact before the degree of infiltration that produces actual deformity has been reached, it is sometimes difficult to distinguish the gouty finger from that of rheumatism. Before the periarticular tissues have been invaded, while the deposit of urates is still confined to the cartilages, the joint exhibits no characteristic

tumefaction. It is merely stiffened, occasionally anchylosed, and a creaking or cracking sound can be heard when it is moved in flexion and extension. The phalangeal skin is thin and drawn down over the retracted tendons, as if all subcutaneous areolar tissue had disappeared. In short, the affected extremity may perfectly present the aspect of chronic rheumatism even at a time when infiltration of the cartilages can be demonstrated by dissection after death. This mimicry of chronic rheumatism is, however, a rather unusual event, and it is among elderly females that it is ordinarily observed. These patients also present another deformity which at first sight may be confounded with the nodosities that in chronic rheumatism are found upon the dorsal aspect of the distal phalangeal joints, and are known as Heberden's nodes. But the gouty tumefaction is located along the extensor tendon of the finger, or upon the sides of a joint; and so dense and immovable is it that it may be easily mistaken for an osteophyte. These little nodes are, however, composed of urates that have been deposited outside of the articulations, without producing any modification in the form or substance of the adjacent bone. In this respect the case differs from chronic rheumatism, for in that disease the phalangeal bones of the affected fingers usually share in the articular swelling. Unlike the smooth and rounded contour of Heberden's nodes, these gouty indurations are often rough and uneven by reason of an unequal and irregular deposit of the urates of which they are composed.

Hybrid swellings of this sort may be sometimes difficult of classification, but there can be no question about the bulky concretions that form around the joints in cases of chronic gout. Layer upon layer the mortar-like deposit gathers in the fibrous tissues, in the cavity and walls of the serous and mucous bursæ, in the sheaths of the tendons, and in the substance of the ligaments, until everything is overwhelmed and ruined by the accumulated incrustations. The resulting form of the diseased joint depends upon the extent of the deposit and the direction of its pressure. Hence great variation in the shape and size of the affected parts. Sometimes the bony structures and sometimes the soft tissues are most severely disorganized, so that there is no uniformity in the changes that occur. In certain cases the whole finger or toe is evenly swelled from end to end, while in other examples the principal deformity is situated upon the sides of the affected joints, and the incrusted tophi are rough and uneven. In many instances these incrustations are somewhat movable, in this respect unlike the osteophytic growths in chronic rheumatism, which are immovably attached to the extremities of the bones outside of the true articular margin. The tophaceous incrustations are usually

situated upon the knuckles of the hand, or near the metatarso-phalangeal articulations of the foot. They sometimes manifest a certain degree of isolation from the joints themselves, and are often connected more intimately with the sheaths of the tendons and the bursæ than with the articular capsule. So long as the skin escapes infiltration it remains thin, smooth, shining, and movable above the subjacent incrustations. But finally, after numerous repetitions of the gouty crisis, the integument becomes infiltrated and adherent to the neighboring tophi. At such points there appear whitish spots which may become ulcerated, permitting the discharge of tophi that are thus loosened by inflammatory action. In the vicinity of these patches the veins are enlarged, so that the participation of the vascular system gives to the whole process an aspect that is truly pathognomonic. The formation of tophi, though usually connected with the course of chronic gout, may also follow an acute attack of the disease. In such cases, it is during the period of decline, as the swelling and pain are subsiding, that a new focus of painful tumefaction suddenly appears outside of the joint, upon the sheath of a tendon, or in a mucous bursa. There is every appearance of an abscess, even to the occurrence of fluctuation, but on incision nothing escapes but a little blood mingled with a pasty fluid that is filled with crystals of sodium urate. After a few days the inflammatory symptoms disappear, and at the end of a month or more the fluid contents of the tumor have dried away, leaving in the soft parts a little hardened concretion, that will serve as a foundation for future incrustations. But in certain cases these minor tophi form at a distance from the affected joint, and it is thus that they are developed upon the ear, the nose, or the forearm, as already described in the section on pathological anatomy. In this way, becoming more numerous after each attack, they may be at last very considerably multiplied, exhibiting an interesting variety of age and stage of development. Sometimes, it happens that tophi which have been deposited during a previous attack are reabsorbed and removed during subsequent attacks, while new ones are formed as if at the expense of the older concretions.

After the formation of a tophus has been completed, the mass usually remains dormant in the connective tissue. Sometimes it gradually increases with the recurrence of each acute attack. In many instances, the skin finally ulcerates over the tumor, and the chalky substance is evacuated very much like the core of a boil; or it may gradually melt down and ooze away in the form of a gritty sero-purulent discharge.

Such is the course of evolution for the tophi that are associated with acute gout. But in the majority of cases their formation is

successive to chronic gout, and is unattended with any considerable amount of pain or constitutional disturbance. A peculiarly indolent variety of tophus is presented by the little dermal concretions that form in the ear, and upon the palmar surfaces of the fingers. When reabsorbed from this latter situation, they leave behind them certain star-shaped cicatrices that are quite characteristic.

The mere presence of uratic deposits in different parts of the body does not necessarily imply extensive injury of the general health. In a certain proportion of cases, on the contrary, the patient is completely broken down, even though the articulations and other parts of the locomotive structures exhibit very little evidence of local disease. This failure of health is the consequence of visceral change affecting the kidneys, the circulatory apparatus, or the respiratory organs. The variety of cachexia that is thus produced depends chiefly upon the predominant form of visceral disease. It is therefore necessary to note the characteristics of visceral gout and the gouty cachexia.

Chronic Gout with Visceral Complications.

Every gouty person is an invalid. Even the robust and vigorous subjects of acute gout can never be ranked as perfectly healthy. And when the disease has assumed its chronic form the patient is a continual sufferer from the presence of urates in the joints and in the tissues elsewhere, as well as from an excess of uric acid in the blood. The vascular walls are the seat of chronic inflammation or of atheroma. The kidneys, the heart, the lungs, the brain—all the organs of the body suffer either directly from local disease, or indirectly from anæmia, toxæmia, and malnutrition. Slowly, but surely, the course of chronic gout tends toward the production of terminal cachexia through the degeneration and utter failure of the vital organs.

The kidneys are usually the first of the internal viscera that exhibit signs of distress. The clinical picture of renal disorder depends largely upon the nature of the concurrent affection of the heart. It is among the once robust and vigorous class of subjects that chronic interstitial nephritis is frequently accompanied by sclerosis of the myocardium and, sometimes, of the liver. These patients pass a considerable amount of urine, especially during the night, which may or may not contain albumin in moderate quantity; the pulse is tense and hard; there are frequent attacks of cardiac palpitation, and sometimes a gallop rhythm is audible over the apex; after a time the heart is evidently enlarged through hypertrophy of its muscular walls, without valvular lesions. During the later stages there is great dyspnœa and precordial distress: the feet swell; dropsy appears;

the flow of urine diminishes, and the symptoms of uræmia usher in the fatal conclusion.

Among the enfeebled subjects of chronic gout renal disease is often accompanied by cardiac symptoms that differ entirely from those that have been just now described. Instead of muscular hypertrophy the heart exhibits dilatation of its cavities, with flaccid walls, and fatty degeneration of the muscular tissue of the organ. Such patients are out of breath on the least exertion, and all their functions are feebly and imperfectly performed. They are pale, and often experience sensations of faintness, dizziness, numbness, and general prostration. In many cases these symptoms are aggravated by the diseased condition of the cerebral and cardiac vessels. The heart frequently beats irregularly and intermittently; its sounds are muffled and indistinct. The pulse, irregular, intermittent, rapid, and feeble, follows suit, and serves to indicate the extent of disorder into which the innervation of the heart has fallen. Death sometimes occurs suddenly, either from cardiac exhaustion or from actual rupture of its degenerated wall. If, however, life be not thus abruptly terminated, the retardation of circulation finally leads to the occurrence of dropsy that is dependent upon the combined effects of renal and cardiac disease. In many instances the phenomena of uræmia are developed; death occurs as the result of this form of intoxication. The approach of uræmia is usually very gradual, and it cannot be mistaken by any one who is familiar with the symptoms of chronic renal disease and the manifold disturbances of the nervous system that follow in its track.

The pulmonary apparatus is sometimes the seat of disorders that characterize the onward progress of a certain number of cases of chronic gout. As age advances, these patients become the victims of dyspnœa and emphysema. Asthmatic paroxysms frequently add to their ordinary and permanent distress. Bronchitis, of an obstinate and interminable character, becomes established. Finally, the walls of the heart give way and the ventricular cavities enlarge. Cyanosis, somnolence, and asphyxia terminate the scene.

Pleuritic effusions, occupying sometimes one side and sometimes both cavities of the chest, are occasionally noted. A passive congestion invades the lungs, and their parenchyma may become œdematous, as a consequence of the general tendency to stagnation of the fluids of the body. Respiration becomes laborious, and the patient dies of slow asphyxia.

No more pitiable object can be imagined than the victim of chronic gout in the last stages of visceral disease. His hands deformed, and his fingers rendered useless through the accumulated tophi; his feet,

lower limbs, and body swelled with dropsy, he can neither stand erect, walk, nor help himself. An excellent appetite leads to overdistention of the stomach, followed by painful dyspepsia. The bowels are constipated; hemorrhoidal veins enlarge; the hips and thighs become brawny from excessive œdema, and the sexual organs are nearly lost from view through infiltration of the scrotum and sheath of the penis. Unable to exercise himself, the patient is confined to an armchair, and soon his whole time is passed in a sitting position, for he cannot lie down without danger of suffocation. Ulcerations form about the tophaceous masses and upon the dependent legs. Paroxysms of dyspnœa, sometimes aggravated by an harassing cough, are accompanied by palpitation or intermission of the heart. Finally, the symptoms of uræmia appear; diarrhœa sets in, sometimes vomiting; occasionally there are epileptiform or apoplectiform convulsions; invincible somnolence overwhelms the sufferer, yet he cannot sleep soundly or comfortably. Only when coma, long desired, arrives at last, is any real relief experienced after years of monotonous misery.

Irregular Gout—Abarticular Gout.

Much discussion has arisen over the possibility of gouty manifestations affecting the internal viscera, either in alternation with or as a substitute for the articular localizations of the disease. With characteristic acuteness of observation the older physicians insisted upon the possible retrocession of articular symptoms and their transfer to an internal organ. Thus a suppression of swelling and pain in the great toe might be immediately succeeded by an asthmatic attack, or by abdominal distress. This is known as retrocedent gout. Conversely, individuals who have suffered long with acid dyspepsia or other visceral disorders find themselves cured of this ailment by the development of an articular inflammation. With the disappearance of articular symptoms the visceral disturbances reappear, constituting what is described as masked gout.

When these different manifestations of disease present themselves thus intimately connected, there can be little doubt of their common origin. But, in order to establish such a relationship beyond cavil, it is necessary to determine the fact of actual experience of gout, either in the person of the sufferer or of his progenitors. Mere experience of acid dyspepsia, of periodical headache, or of any other of the allied disorders, is not sufficient to warrant the assumption of the term *masked gout*. These symptoms must occur in the person of a member of a gouty family, or they must be dissipated by the appearance of articular disease, before they can be assigned to that rank. As

to the phenomena of *retrocedent gout*, there can be scant space for uncertainty when the sudden and premature subsidence of articular inflammation is immediately followed by violent disorder in an internal organ. The dangers that attend such retrocession are usually determined by the location and intensity of the disturbance that is thus transferred from the merely locomotive organs to the vital structures of the body.

The possibility of masked forms of abarticular or visceral gout is now generally admitted. In many instances these visceral manifestations exist for many years before the appearance of articular disease, and, apart from a history of heredity, constitute the only indications of the arthritic diathesis. In many instances, also, when the causes that lead to articular crises have been avoided by the practice of temperance and wholesome living, visceral accidents may throughout the whole of life recur in periodical fashion, and may never be replaced by the acute or chronic articular forms of gout. This attenuated gout is not uncommon among the temperate descendants of a gouty ancestry, and its phenomena have been described as the consequences of *lithæmia*, a euphemism that appears to have been invented for the purpose of sparing the morbid sensibility of the patients.

Visceral Gout Affecting the Digestive Organs.

Among the subjects of the arthritic diathesis it is a common thing to meet with disorders of the alimentary canal and its appendages; and it is not always easy to distinguish between gouty affections of the digestive apparatus and accidental maladies that have no special relation with the diathesis. It will, however, be useful to pass in review the principal diseases that are frequently encountered among those who have either inherited the gouty predisposition or have already experienced its crises. Pharyngeal inflammations are usual among all sorts of people, but among children and young people who subsequently suffer with arthritis it is a frequent event to meet with chronic inflammation of the pharyngeal mucous follicles. Sir Dyce Duckworth says ("A Treatise on Gout," p. 88): "The gouty throat is like no other. The pillars of the fauces, especially the posterior pair, the velum, and the uvula, are very red and glazed. . . . The uvula is greatly enlarged and elongated, sometimes seeming to fill up the gap between the pillars. It has often an œdematous border . . . and tip. . . . The surface of the latter (pharynx) is not so smooth as that of the fauces. It is coarse, with red, glairy prominences upon it, and depressions here and there covered with grayish, slightly adherent patches of mucus, and it has sometimes enlarged

venules upon it. In elderly people the redness is less marked." Sometimes concretions of calcium carbonate and urate are discharged from the enlarged mucous follicles of the pharynx.

Another frequent event among the gouty is acute suppurative tonsillitis. This sometimes recurs with a regularity that equals that of the genuine articular attacks. Sometimes an attack of gout is ushered in by severe inflammation of the tonsil. With certain patients the acute crisis always commences in this way. In other cases the attack is preceded for several days by slight pharyngeal redness, accompanied by somewhat painful deglutition which, at the end of five or six days, disappears and is succeeded by ordinary articular signs.

Occasionally it happens that a spasmodic stricture of the œsophagus is experienced by the arthritic subject. This usually occurs in nervous patients who are dyspeptic and somewhat neurasthenic. It sometimes immediately precedes an acute articular attack, and disappears with the evolution of its paroxysms. But it may occur independently of the attack, and it is usually experienced during the act of eating. It is often associated with precordial oppression and great anxiety. Its duration is usually brief, occupying only a few minutes, and it is often terminated by the regurgitation of liquids that have been recently swallowed.

The obscurity that surrounds the relationship between these affections of the pharynx and the œsophagus and genuine gout does not involve its connection with disorders of the stomach. The majority of the subjects of hereditary gout are victims of gastric disease. Long before the explosion of articular gout, they have had chronic and painful experience of manifold forms of indigestion. But it is impossible from these signs alone to recognize an arthritic predisposition—the family history, or some previous malady of the arthritic type, is necessary to the establishment of an etiological diagnosis. As a general rule, however, gouty dyspepsia is marked by gastric pain. There is a sense of distention after eating; there is flatulence and more or less acid eructation; digestion is retarded; attacks of gastralgia are not uncommon, and in many cases a burning sensation in the epigastrium is frequently felt. These various symptoms may be grouped in two principal classes: in the first, the phenomena of atonic dyspepsia and auto-intoxication are most prominent; in the second, the symptoms of chronic gastritis chiefly engage the attention. In the atonic form, there is loss of appetite, sometimes amounting to a real disgust for food. After a meal there is some swelling of the epigastric region, accompanied by feelings of constriction and weight about the stomach; for two or three hours an inclination to

sleep, and an evident loss of the power of attention and application to business are apparent, but there is no considerable pain. In the catarrhal form, there are distressing eructations that may be either acid or bitter, and burning. Violent pain and cramps are felt in the region of the stomach, sometimes radiating into the cardiac area and interscapular space. Nausea and vomiting sometimes occur to a degree that renders it impossible to take food. Frequently a considerable quantity of glairy mucus, sometimes streaked with blood, is thrown up from the stomach. Sometimes these evacuations are daily occurrences; while in other cases, especially when characterized by gastric dilatation, a large amount of offensive liquid of a yellowish or greenish color is vomited at intervals of three or four days. All these symptoms, however, may be exhibited as the result of simple indigestion, and there is nothing in their evolution that is pathognomonic of gout. It is only the frequent association with the diathesis that is remarkable. For this reason many able authors have denied the existence of anything more than accidental connection between gout and gastric disorder. Such writers usually express great incredulity regarding the existence of an arthritic diathesis. But it seems impossible to reconcile such opinions with the facts that are revealed by a large clinical experience where the causes of arthritism are continually operative. Dealing with patients who are past the middle of life, and who are confirmed gluttons or drunkards, it is easy to formulate the belief that all their gastric symptoms are the direct consequence of persistent intemperance in the matter of eating and drinking. But there is another large class of chronic dyspeptics who are of gouty lineage, yet who, by reason of intelligence and forethought, have avoided the exciting causes of acute arthritism, and have never experienced an articular attack, but are continual sufferers with dyspepsia that is identical with that which is experienced by their imprudent companions who are victims of unimpeachable gout. When, in advanced life, such people are finally attacked with articular crises, the complete disappearance of their gastric disorders is an event too notable and too intimately associated with the outbreak of gout to admit of anything but the conviction that these are two alternating phases of the same disease.

In this belief the great clinical teachers are agreed. Additional evidence pointing to the same conclusion is afforded by the cases in which the cessation of recurrent articular attacks is followed by recurrent paroxysms of gastric distress which are repeated, sometimes at regular intervals, until they are terminated by the renewal of articular manifestations. The acceptance of this doctrine regarding the relation that exists between gout and dyspepsia should not diminish

the caution with which the investigation of individual symptoms is approached. In certain cases the disorder of the stomach is the consequence of renal disease, and is one of the modes of expression by which the occurrence of uræmia is declared. In many instances the exciting cause may be found in excess of eating and drinking, or in the indigestible quality of the food. But, behind all these exciting causes a careful research will seldom fail to discover an intimate connection with the obscure errors of nutrition that underlie the gouty diathesis.

The rather rarely observed phenomena of retrocedent gout are still regarded with considerable skepticism by many writers. Certain traditions are recorded in the standard works, relating the histories of reckless patients who, in order to assuage their pain, have soaked a gouty foot in ice-cold water, to the immediate relief of acute inflammation, and an immediate appearance of violent gastralgia, precordial distress, dyspnœa, hiccough, vomiting, and collapse. These formidable symptoms are generally dissipated by copious evacuation of the bowels, or by a return of inflammation to the deserted joint. A flood of ink has been shed in the effort to discredit the apparent connection between these consecutive events; but still it remains impossible to disabuse the mind of the unbiased observer who has witnessed such a case, of the belief that there is something more than a merely accidental connection between these facts of retrocession. Especially convincing are those rare cases in which articular inflammation is interrupted by a gastric crisis, and is resumed again so soon as the stomach is relieved. The bare fact that after death the gastric mucous membrane exhibits all the signs of acute local inflammation does not militate against the theory of retrocession, for daily experience and observation show how rapidly a gouty joint develops the evidences of acute inflammation, and the same thing may occur in the stomach. It is true that in certain cases, complicated with renal disease, violent vomiting and collapse may be excited by uræmic intoxication; but these are usually witnessed among the victims of chronic gout, and there is nothing of an acute character in their articular affections. When the stomach exhibits after death the signs of chronic inflammation, they must be accepted, of course, as evidence of chronic gastric disease; but that need not preclude the idea of an acute attack engrafted upon an old worn-out stem, if the articular disease be suddenly suppressed. The rarity of an event is no proof of its unreality; retrocedent rheumatic peritonitis, for example, is an uncommon incident, yet it does sometimes occur. In short, while admitting the fact that gastric disorder dependent upon its usual exciting causes may accidentally concur with an attack of gout, begin-

ning a little sooner or a little later than the articular crisis, it must still be insisted that there is in the nature of things no reason why retrocession may not occur, and that there is sufficient testimony on the part of trustworthy witnesses to warrant the belief that it does occasionally take place.

The same arguments have been used for and against the existence of intestinal gout. It is not an unusual experience for gouty subjects to suffer with a catarrhal condition of the intestinal canal without much regard to the character of their diet and mode of life. As in other forms of catarrhal enteritis, the action of the bowels is very irregular; sometimes constipated, flatulent, and colicky, and again relaxed, with frequently recurrent diarrhœa that continues for several days and then spontaneously ceases. Sometimes, however, there is persistent and obstinate looseness of the bowels, which continues for many years without pain or noteworthy injury of the general health. It is liable to intermission, and to recurrence in the spring and autumn months. In many instances it is preceded by severe colic, flatulence, headache, and deposit of urates in the sediment of the urine. In these preliminary disorders it bears a close resemblance to the crises of articular gout; and frequently it is clearly alternating with such attacks. The resemblance is further carried out by the relief that is afforded and the improvement of health that is experienced after such evacuations. But when diarrhœa becomes permanent, it, in association with other visceral complications, seems finally to debilitate the chronic sufferer. Among gouty subjects it is frequently remarked that catarrhal inflammations of a migratory character are not uncommon. In such cases there is often observed an alternation between bronchitis, or asthma, and catarrhal diarrhœa—one form of mucous disease taking the place of another, and all of them related to other diathetic manifestations in a way that seems conclusive as to the community of their cause. Witness such facts as are related by Scudamore, Graves, and other clinical teachers who have noted the effects of exposure to wet and cold during an attack of articular gout—suppression of local symptoms, immediate occurrence of intestinal pain, constipation, hiccough, flatulence, and other evidences of abdominal distress—in a word, retrocedent gout. Sometimes the focus of the disorder is about the head of the colon, in the right iliac fossa, and it has been in certain cases incautiously ascribed to appendicitis; but usually the pain is unattended by fever, and is relieved by a summary cathartic and a few doses of sodium salicylate. Sometimes, however, retrocession is accompanied by fever and symptoms of acute intestinal inflammation. When this chiefly involves the small intestines there is a copious watery flux like that of cholera

morbus. It was an attack of this character that terminated the life of the great Sydenham, on the 29th of December, 1689. When the descending colon and the rectum are affected, the discharges are scanty, slimy, mixed with blood, and attended with tenesmus, like those that occur in genuine dysentery. Severe hemorrhoidal attacks are also commonly associated with the gouty predisposition, and sometimes appear to replace the ordinary articular crises.

Despite these facts, one must not fall into the error of ascribing all cases of diarrhœa or dysentery or intestinal colic in a gouty person to masked or retrocedent gout. The same caution must be exercised that is demanded in the corresponding forms of gastric disorder. Arthritic patients may have the same diseases, excited in the same way, that are experienced by other people. It is only when the phenomena of articular inflammation and intestinal disorder are so intimately related that they clearly replace one another, and are habitually interchangeable, that we are justified in claiming the identity of their cause.

Hepatic Changes.

The effect of gout upon the liver is unquestionable, but the nature of the connection is not placed beyond dispute. Murchison and his followers have gone so far as to place the original cause of gout in the liver, while others, on the contrary, seem disposed to exculpate that organ from everything but a slight tendency to hyperæmia and disordered function during the paroxysms of the disease. Between these extremes lies the truth. It may be safely asserted that the liver of an individual who has either inherited or acquired the arthritic diathesis is never perfectly healthy. The important part that is taken by the organ in the elaboration of urea and its congener, uric acid, renders it certain that the conditions which exaggerate or derange the processes by which nitrogenous refuse is evacuated from the body cannot fail to implicate the liver as well as the kidneys. This will be more fully discussed in the section on the pathology of gout.

A tendency to hyperæmia of the liver accompanies acute attacks of gout. The organ is distinctly enlarged and projects below the short ribs. It is often quite sensitive to pressure on such occasions, but during the interval between attacks it loses in great measure its sensitiveness, and returns to its normal volume. In fatal cases of acute uncomplicated gout, the liver presents nothing remarkable, nor does it contain urates, even though the joints may be loaded with them.

But in many instances during life there is abundant evidence of chronic inflammation or of cirrhosis of the liver. The liver of a

gouty person is not less liable to ordinary hepatic diseases than that of another individual. The mode of life and the habits of the patient have been usually of a character to induce chronic or even acute hepatic disease. Consequently, it is to be expected that upon the autopsy-table the liver will frequently exhibit evidences of disease that are due to intemperance in eating and drinking rather than directly to the action of gout. As a matter of fact the gout and the diseased condition of the liver are both of them results of the dietetic and hygienic errors of the patient himself or of his ancestors. They own a common cause, and they may exaggerate each other.

The strong tendency to catarrhal inflammation of the mucous surfaces of the body exhibits itself in the biliary canals as it does in the respiratory passages. In many cases jaundice from catarrhal obstruction is a pronounced feature. This may exist through the extension of inflammation from the duodenal surfaces, or it may be the consequence of biliary lithiasis, a condition that frequently occurs among arthritic subjects.

As a result of the hepatic disorders that afflict the gouty, intestinal dyspepsia is of frequent occurrence. Slight errors in diet, exposure to cold, and unusual fatigue very commonly excite in the over-sensitive organism the phenomena of hepatic indigestion. There is loss of appetite, a bad taste in the mouth, a yellow tongue, and a feeling of uneasiness that begins about an hour after eating, and is accompanied by intestinal flatulence, rumbling, and discomfort. Usually these symptoms persist until relieved by a spontaneous diarrhœa of short duration, or by the action of a cathartic, or by voluntary fasting followed by a change of diet on the part of the patient.

Gouty Affections of the Circulatory Apparatus.

Cardiac diseases are very frequent among arthritic subjects, but it is often difficult to decide between gout, rheumatism, and other diseases as to the part they respectively play in the causation of the particular cardiac disorder that may be in question. In the majority of cases the disturbance is of a functional character; but there is, besides, a considerable number of examples of genuine organic disease of the heart.

Cardiac palpitation, without permanent lesion of the organ, is sometimes noted at the outset of an acute attack of gout. This usually occurs among the earlier manifestations in youthful subjects whose viscera have not yet been damaged by chronic disease. The paroxysm of palpitation usually occurs, without considerable pain or alarming conditions, during the night; and on rising in the morning

the great toe is seen to be swollen, and the heart is relieved. True cardiac inflammation never supervenes upon such an attack.

Somewhat similar irregularity of the action of the heart is frequently experienced during the intervals between the attacks of gout. The patient is often oppressed by a feeling of precordial distress, accompanied by violent beating of the heart. As a matter of fact, such symptoms are seldom encountered among vigorous young men who are neither anæmic nor given to excessive use of tobacco, unless they are predisposed to rheumatism or gout. It must be remembered that one of the characteristics of the arthritic diathesis is a predisposition to disorders of the digestive apparatus. Now the nervous connections between the stomach and liver and the heart are so intimate that indigestion cannot fail to disturb the cardiac functions. Consequently, the commotions to which the heart is liable under such conditions may be considered primarily as the result of dyspepsia, and secondarily as the outcome of the gouty dyscrasia. In severe cases the act of gastric digestion is accompanied by flushing of the face, tumultuous irregular intermittent pulsation of the heart, with precordial oppression, and sometimes a degree of pain that is suggestive of angina pectoris. But with the completion of digestion agitation subsides, and the heart beats normally until the next meal.

Such being the violence of the disturbance that is excited among youthful and comparatively healthy subjects, it is easy to comprehend the gravity of the disorders that exist when the worn-out heart of an aged, obese, and atheromatous arthritic is in question. In such cases there is almost constant irregularity and frequent intermission of the movements of the heart, as the result of irritation propagated from the stomach and the liver through the medium of the nervous system, and especially as a consequence of intoxication with the products of gastro-intestinal fermentation, and with nitrogenous refuse (urates, etc.) that has been retained in the circulating fluids of the body. Under the influences of these hindrances to healthy nutrition the muscular substance of the heart falls into a condition of progressive degeneration; the ventricular cavities become dilated; with every fresh attack of gout the organ grows weaker, until at last all healthy function is rendered impossible. Cardiac asthma, stagnation of the blood, passive engorgement of the liver, œdema, general dropsy, universal embarrassment of function, collapse, and death, follow each other in inevitable succession.

The paroxysmal recurrence of cardiac asthma constitutes one of the most frequent and formidable evidences of masked gout. Sometimes accompanied by a copious bronchial flux, there may suddenly arise great danger of immediate suffocation. In other cases, the col-

lapse of the cardiac musculature itself induces fatal syncope, or at least an alarming prostration accompanied by an almost complete arrest of the circulation.

Besides the morbid changes thus indicated, the ventricular walls are liable to hypertrophy in cases of gout that are characterized by a very trifling deposit of urates about the joints. In such cases the disease appears to expend itself chiefly upon the internal viscera, producing chronic interstitial inflammation of the kidneys, liver, and heart. During the later stages of chronic gout, especially after the nutrition of the heart has been checked by atheroma of the coronary arteries, the muscular substance of the organ undergoes fatty degeneration, and this may lead to rupture of the ventricular wall, or to fatal syncope through the utter failure of the contractility of the cardiac tissues.

Retrocession of gout from the extremities to the heart is a rare incident, but there are well-attested cases of this accident. As a consequence of refrigeration of the inflamed joint, or of violent agitation of mind and body, swelling and pain have abandoned the affected member, and their disappearance has been speedily followed by cardiac collapse. It is probable that in such instances the overwhelming disturbance of the heart is due to perturbation of the nervous centres, and to over-stimulation succeeded by paralysis of the cardiac excito-motor nerves. The debilitated condition of the organ and the inordinate irritation of its nervous tissue, consequent upon chronic arthritism, must not be forgotten in estimating the causes of collapse under such conditions.

The influence of gout in the production of atheroma in the arteries is beyond question. Yet, like the course of arthritic degeneration in other structures and organs of the body, it is often the case that atheroma is the result of the causes that have also produced gout, rather than the direct consequence of gouty disorder.

So many factors may contribute to the production of arterial degeneration, such as old age, intemperance, errors of diet, etc., that it is sometimes difficult to assign to each its exact share in the work of destruction. The remote consequences of an atheromatous condition of the blood-vessels are very numerous, and when that condition is due to gout or to the arthritic diathesis, they may be reckoned among the secondary or remote results of arthritism. Thus, for example, thrombosis and hemorrhage in the brain may follow disease of the cerebral arteries. In the heart, an atheroma of the coronary arteries leads to starvation, degeneration, and rupture of the cardiac muscle. Gangrene of the extremities has also been attributed to a corresponding state of the vascular walls in the limbs, but the com-

paratively frequent occurrence of diabetes as the antecedent of such mortification should lead to careful inquiry as to the possibility of that as the cause. The connection between diabetes and the arthritic diathesis is, however, so intimate that in many instances gangrene, glycosuria, and gout can all be referred to the same predisposing cause or causes.

Angina pectoris is an incident of not infrequent occurrence among gouty patients. It is usually experienced by the victims of chronic arterial degeneration in whom the aorta has become atheromatous. The onset of an attack is often the first indication of the existence of the disease that has insidiously undermined the vitality of the vascular tissue. It may be an unusual muscular effort or a fit of indigestion that excites the first paroxysm of pain; but the real anatomical cause consists in the altered structure of the atheromatous vessel.

True angina pectoris thus originated is a far more serious incident than its counterfeit, that form of cardialgia that occurs among youthful subjects who have not yet acquired an atheromatous degeneration of their arteries. Such patients, as a consequence of indigestion, or of the excessive use of tobacco, tea, or coffee, may suffer severely with attacks of intensely painful neuralgia in the precordial region. The paroxysm is characterized by violent pain and a feeling of constriction about the inferior portion of the thorax. Painful irradiations penetrate the interscapular space, and sometimes reach the neck and shoulders, or extend into the arms, and follow the track of the nerves as far as the tips of the fingers. Breathing seems difficult; perspiration covers the surface of the body; the face is pallid and expressive of the utmost anxiety and distress. The pulse is small, rapid, and feeble, so that the tips of the fingers grow cool. Everything testifies to the existence of arterial spasm, rather than the loss of contractility that follows degeneration of the arterial coats. After a variable period of suffering the paroxysm subsides, unless cut short by therapeutic measures, and all goes on as before. Such experiences are frequently connected with ordinary dyspepsia, but they are also common among the gouty. During the early stages of the disease, such attacks often precede and usher in the articular crisis; and they are not uncommon among neurotic members of the arthritic family long before the occurrence of articular manifestations. These early neuralgic pseudo-anginas are rarely attended with danger, but the genuine form of angina pectoris is usually fatal—if not at the time of the first attack it may destroy life in any subsequent paroxysm. Post-mortem section reveals chronic inflammation of the aortic walls with atheroma and constriction of the lumen of the nutrient arteries of the heart. In such cases death is the result of an

arrest of circulation in the cardiac wall, and it is only indirectly connected with gout. Thus produced, death is the direct consequence of arterial disease, and should not be ascribed to retrocession of the articular disease.

The veins are usually affected by serious changes during the progress of gout. The dilatation and varicosity of the veins in the vicinity of the inflamed joint have been already noted. Sometimes this condition persists in a greater or less degree after the termination of an attack, and tends to become permanent and to involve the majority of the vertical veins in the lower extremities. Besides growing varicose, the veins are very liable to inflammation, which is developed during or after an articular crisis, or as the consequence of some trifling injury—like a bruise or a blow. Phlebitis of this character is often transient in its manifestations, progressing from one segment to another of the affected vein, and remaining nowhere fixed for any considerable time. In many cases, however, it pursues the course of an ordinary inflammation without any unusual peculiarities. Its recognition is easy when a superficial vein is involved, but when the deep veins, in the calf of the leg for example, are inflamed, the fact is made known by the existence of deep-seated pain along the track of the vessel, and by an œdematous condition of the limb. In one notable fact gouty phlebitis differs from the ordinary form of the disease—in its tendency to relapse without apparent local cause. Sometimes the inflamed vein becomes permanently closed, causing persistent œdema of the limb that is exaggerated by standing or walking; but usually there is more or less complete recovery. Occasionally, as in ordinary cases, embolic accidents occur, and fatal obstruction of a pulmonary vessel may follow the detachment of a fragment from the thrombotic plug.

The tendency to phlebitis is evidently hereditary in certain families. In this respect it resembles the gouty diathesis, upon which in such cases it is undoubtedly dependent. Whenever, in comparatively youthful male subjects, the veins become inflamed without apparent cause, there is reason to suspect gouty antecedents and predispositions, and the line of investigation should, accordingly, be guided in that direction.

The Respiratory Organs.

The influence of gout upon the respiratory apparatus is not always clear. The laryngeal cartilages and ligaments are occasionally invaded by a deposit of urates, but it is very seldom that any of the spasmodic or suffocative phenomena of ordinary laryngitis or œdema of the glottis are experienced in such cases. A certain degree of

hoarseness and weakness of articulation may be remarked, however, as a consequence of obstruction of the movement of the cartilages through chronic thickening of the laryngeal membrane, and infiltration of the cartilaginous structures themselves.

The respiratory passages are liable to inflammation of obstinately persistent character, and to attacks of asthma that either coincide with attacks of gout, or appear to alternate with them. The tenacity with which bronchitis clings to the gouty has been long recognized. It is characterized by a tedious, dry cough, with comparatively little expectoration, but accompanied by considerable feeling of pulmonary oppression. In many instances this chronic inflammation finally terminates life by invasion of the terminal bronchi, and the development of the phenomena of capillary bronchitis. Sometimes the last stage of the malady is complicated by effusion into the pleural cavity, or by the evolution of acute pulmonary œdema. There has been considerable debate regarding the nature of bronchitis among the gouty. Some have insisted upon a specific character by which it can be differentiated from all other varieties of bronchial catarrh, while others are equally positive in the statement that bronchitis is merely bronchitis whether it occur among the gouty or among those without arthritic predisposition. Aged people are liable to a chronic cough, with trifling expectoration, that persists for many years, so long, in fact, as life may endure. It has been claimed with good reason that this is often the result of exposure and neglect of ordinary precautions against catarrhal inflammation; still, in a large proportion of cases, careful analysis will bring to light a decided diathetic substratum for such a cough. Sometimes an acute attack of gout is preceded or accompanied by an acute bronchial catarrh that soon disappears after the establishment of the articular crisis. Such cases are always open to the objection that they were simply accidental coincidences; but in chronic gout the connection between the primary disease and the respiratory malady is far more intimate and conspicuous. It is among the advanced cases in which the kidneys and the liver are becoming sclerosed that the emphysematous lungs are farther embarrassed by the establishment of chronic bronchitis. These patients, with or without articular incrustations, gradually evolve the well-known signs of emphysema and bronchitis. The chest becomes barrel-shaped and resonant; respiration is rendered hurried and laborious by the slightest exertion; perspiration trickles from the surface after the least effort, and is followed by chilliness, if there be any exposure to even the most moderate current of air. The changeable weather of spring and autumn is fraught with danger for these sensitive subjects. They take cold with the first sudden change at the end

of summer, and their coughs usually persist until the close of the next spring. Even during the intervals between the periodical attacks, it is usual to find bronchial râles audible over the posterior and inferior portion of the chest.

So far as the physical signs and the expectoration are concerned, there is nothing pathognomonic about the bronchitis with which the gouty are afflicted. It is its association with other evidences of arthritism, its persistence, and its occasional alternation with articular manifestations that give it distinction. It is aggravated by many of the causes that operate unfavorably upon the gouty condition. Sometimes it is worse during the heat of summer, when the arthritic constitution exhibits that tendency to exhaustion that is so often manifest during the sultry days in the earlier and later portion of the hot season. Sometimes it is relieved by a humid state of the atmosphere. It is often made worse by anxiety and fatigue of mind or body.

Among arthritic subjects there is often a notable relation between chronic bronchitis and certain obstinate cutaneous eruptions that belong to the arthritic group of diseases. With the disappearance of one, the other is aroused to activity. Thus, it is recorded of the great Napoleon that having been harassed for a long time by an obstinate cough, he was at last persuaded by Josephine to consult her favorite physician, Corvisart. On investigation it appeared that the bronchial affection was coincident with the suppression of an old eruption that had existed for many years. Corvisart immediately ordered a course of counter-irritation, which soon revived the cutaneous malady and cured the cough. Chronic gouty bronchitis is sometimes accompanied by sudden paroxysms of spasmodic dyspnœa that are out of all proportion with the physical signs that are afforded by auscultation. These attacks are frequently induced by the recumbent position, and are relieved by sitting up, or by the inhalation of the vapor of ether. In elderly subjects, however, the possibility of a uræmic cause for such paroxysms should never be forgotten, and they should be the signal for careful supervision of the course of events in the kidneys and heart. Chronic interstitial nephritis and cardiac dilatation will be often discovered as the proximate cause of such respiratory dyspnœa.

The gouty character of these varieties of bronchitis can hardly be questioned when they are associated with the usual articular manifestations; but when bronchitis precedes these changes, the connection is more obscure though none the less real. The respiratory malady is in such cases rightly estimated as a masked variety of gout.

Nervous or spasmodic asthma is often associated with the gouty diathesis. In many instances it alternates with or replaces the habitual articular attacks. Of course there are numerous asthmatics who are never gouty, but there are, besides, many arthritics who exhibit the phenomena of asthma in such close relation with their diathetic attacks that it is difficult to doubt their common causation. Such cases are encountered in gouty families where numerous ancestors have transmitted the history of all possible modes of arthritic disease, and have exhibited all the affiliated disorders without interruption. In such families asthma is of frequent occurrence, either as an antecedent or as an alternative affection. Yet so long as there is no recorded case of retrocedent gout actually replaced by an asthmatic attack, it may be proper to speak of asthma as the expression of a morbid tendency that frequently accompanies gout, though not itself a manifestation of that disease.

The pleuritic effusions that are sometimes witnessed in gouty patients are probably only very indirectly connected with the disease. They occur as a consequence of ordinary exposure to cold, and their character differs in nothing essential from the ordinary varieties of pleuritic inflammation. The same thing may be said of the attacks of pneumonia that sometimes occur in gouty subjects. This might be expected, since pneumonia is not the result of intoxication, but of a specific infection. But the transient attacks of pulmonary hyperæmia, that are sometimes accompanied by expectoration of blood, in non-tubercular subjects, are often connected with gouty disorder, and have no more importance for prognosis than the hemorrhoidal fluxes with which they sometimes alternate.

The Nervous System.

The influence of gout upon the nervous system is beyond question, yet there is no department of pathology that presents a greater number of difficult problems than that dealing with the nervous phenomena associated with gout. So many and so various are the morbid changes that affect the principal organs of a gouty patient that it is often a matter of extreme delicacy to decide what is due to masked or retrocedent gout, and what must be ascribed to a diseased kidney or other disabled apparatus. Thus, it being not unusual for gouty subjects to suffer with chronic interstitial nephritis, the intercurrence of cerebral symptoms calls for careful discussion of the possibilities of uræmia as the cause of the nervous disturbance. It is well known that interstitial nephritis may progress insidiously without notable symptoms until a sudden and violent explosion in the midst of ordinary

apparent health unmasks the fact of disease. If now the patient has been subject to the prodromes of gout, or to an occasional articular crisis, it is very natural to ascribe to that disease, in either its latent or retrocedent varieties, the apoplectiform seizure, the epileptiform convulsion, the violent headache, the delirium, or the coma by which he is prostrated. But examination of the urine, indicating the presence of casts and albumin, or a post-mortem section of the body, will usually refer such accidents to their source in a ruined kidney.

Disease of the cerebral arteries is a frequent cause of death among gouty subjects. Here, again the phenomena of hemorrhage and compression of the brain might be mistaken for retrocedent gout, or for uræmic coma. At the bedside, without full knowledge of the history and antecedents of the patient, the problem sometimes assumes great difficulty.

In like manner, the concurrence of an attack of delirium tremens with an imperfectly developed crisis of gout might easily lead to the belief that the brain was suffering from the incidence of retrocedent articular disease.

But, in spite of the fact that very many of the cerebral accidents that occur among the gouty can be referred to causes other than gout, it still remains true that violent disturbances of the brain may be excited by sudden suppression of the articular manifestations during an ordinary attack. Cases have been recorded in which the sufferer has sought to ease his pain by plunging the feet into cold water, with the result that disappearance of local pain and swelling in the foot has been promptly followed by violent headache, disturbances of vision, vertigo, and somnolence, or even by still more alarming symptoms of apoplexy, hemiplegia, and coma. In such cases active revulsive treatment, with leeches, mustard applications, and purgatives, has sometimes been rewarded with the renewal of articular swelling and pain, and the complete disappearance of all cerebral phenomena. Similar evidences of retrocession have been sometimes witnessed as a consequence of great fatigue and violent emotion; but it must not be forgotten that under such conditions old people occasionally become temporarily delirious and prostrate without the existence of arthritic manifestations.

An interesting fact in connection with the cerebral disorders of the gouty is the frequent occurrence of aphasia. This sometimes occurs merely as a consequence of failing nutrition of the brain, but in certain cases it clearly alternates with the articular phenomena. Sometimes it is accompanied by convulsive spasms of the facial muscles and upper extremities, which are generally unilateral in their manifestation. Genuine epilepsy is almost always aggravated by a gouty

habit of body, but sometimes it completely disappears after the development of acute articular gout.

These violent disturbances of the brain are, however, the exception rather than the rule. In the majority of instances, only the milder varieties of nervous disorder are encountered. Headache, usually in the form of hemicrania, is a common experience among the gouty. Sometimes it alternates with the joint affections; sometimes it persists for weeks and months until dissipated by an articular crisis. Vertigo, either with or without headache, is also of frequent occurrence and similar behavior. It is probably dependent in certain cases upon gastric disorder, and in others upon a diseased condition of the cerebral vessels.

Mental disorders are sometimes witnessed in gouty subjects. These disturbances are usually modified in accordance with the temperament of the individual, so that the sufferer sometimes exhibits only the most wonderful patience and amiability throughout a lifetime of disease. But in the majority of cases the irascibility of the patient is something phenomenal. Depression of spirits, hypochondria, and excessive irritability are generally experienced. In this respect the state of the brain conforms to the general condition of morbid excitability and debility into which the entire organism has fallen. Gouty insanity has been described by many authors; but such an event is of rare occurrence, so far as alternation with gout or substitution for gout is concerned. Doubtless, many insane people are gouty, and the depth of despair into which many gouty patients are plunged may lead to some confusion in the analysis of symptoms. It is often difficult in these cases to draw the line between actual insanity and the various forms of nervous perversion that may arise during the course of articular disease. Still it is unnecessary to ascribe to gout the different neuroses, such as chorea and hysteria, that may be associated with it. This should be done only when the facts of alternation and of substitution of one for the other are beyond question, and when independent morbid conditions and lesions of the nervous structures cannot be discovered. An exception should be made, however, in favor of hemicrania. This singular neurosis so constantly occurs in gouty families, is so frequently experienced among the precursory phenomena of the arthritic diathesis, and is so clearly connected with the articular crisis that its relationship does not admit of question.

From this brief view of the cerebral accidents of gout, it is evident that there are many points of resemblance between it and cerebral rheumatism. There is the same retrocession of articular manifestations, the same violent onset of cerebral disturbance, the same ten-

dency to delirium, coma, and death. On the reverse of the picture, however, aphasia, which is so common in cerebral gout, is an exceptional event in cerebral rheumatism. Vertigo belongs to gout, while delirium, convulsions, and excessive elevation of temperature are more frequently witnessed in rheumatism. In both diseases the post-mortem appearances are insignificant and out of proportion to the gravity of the symptoms by which they are accompanied.

It is very doubtful whether the spinal cord is ever the seat of genuine gouty inflammation. Gouty subjects have suffered and died with myelitis, but there is no satisfactory evidence that this differed in any particular from ordinary inflammation of the spinal cord. The unique case, recorded by Ollivier, in which there was a general deposit of urates upon the external surface of the dura mater and the sheaths of the spinal nerves, shows that the fibrous tissues within the spinal canal can be damaged by infiltration. But in this case the cord and its inner envelopes remained healthy. If the spinal cord ever becomes diseased through gout, it must be the result of indirect influences like those that excite sclerosis in the kidney, heart, blood-vessels, liver, and spleen. It is also probable that the transient feeling of weakness in the lower limbs that is sometimes experienced by gouty patients has its origin in fugitive disturbances of nutrition that are really dependent upon gout. There is no reason why the poison of gout, like that of syphilis, should not create a predisposition to chronic myelitis; and when no other cause of inflammation can be discovered, the affirmative inference becomes unavoidable.

With similar reservations the influence of gout upon the peripheral nerves is incontestable. Neuralgias of the greatest severity and obstinacy are among the most frequent consequences of gout. By their recurrent and paroxysmal manifestations they often resemble the evolution of articular gout. No part of the body appears to escape their incidence, and their duration varies from that of the most transient fulgurant pain to the unintermitting and persistent agony of chronic inflammation. Chief among the disorders is sciatica, which may occur either as a simple neuralgia or as an uncompromising neuritis. It is occasionally accompanied by anæsthesia and muscular atrophy, but usually the principal symptom is pain along the course of the sciatic nerve and its branches. It is extremely liable to recurrence and to frequent exacerbations without apparent cause. Sometimes it alternates distinctly with articular manifestations; but more frequently it seems to be excited by accidental exposure to cold or injury.

Neuralgias of the trifacial and intercostal nerves follow sciatica in the order of frequency. The writings of the English are rich in de-

tails regarding these peripheral pains, which are usually worse at night, and are clearly connected with the prodromes of articular gout. Sometimes they cannot be clinically distinguished from the pains of muscular rheumatism, and they may assume the forms of lumbago, or of deltoid or crural pain. The recti abdominis muscles are frequently thus affected. Occasionally, pain is experienced in the tongue or about the teeth, usually fugitive in character, but sometimes yielding only after weeks of suffering. Sometimes it is in the deep muscles of the spinal column that pain is felt, or it may occupy the track of any deep nerve, especially at night, causing unusual sensations, as if an almost intolerable cutaneous itching had been transferred from the surface to the central tissues of the part. In many instances, fortunately, these torments are very fugacious, but sometimes they manifest a degree of prominence that is suggestive of subacute peripheral neuritis. When they are encountered in robust and vigorous subjects, they usually yield to vegetable diet and purgatives, followed by colchicum and sodium salicylate; but among aged and broken-down subjects they are the result of permanent degeneration of tissue, and are seldom relieved by medical treatment without recourse to surgery.

Besides the sensory disorders above indicated, the peripheral nerves are also subject to motor disturbances that take the form of muscular spasm, involving sometimes an individual muscle, and sometimes arousing a whole group of muscles. The spasms are of very frequent occurrence among the introductory symptoms of a gouty attack; they are often experienced during the intervals between the paroxysms of the disease, and with advancing years they become one of the most tormenting incidents in connection with chronic gout. In certain cases, they are so often repeated and are attended with such a degree of exalted reflex excitability, that they seem to be dependent upon morbid changes in the spinal cord. Probably, however, they simply express the general condition of irritable weakness into which the entire organism has fallen. Even among arthritically predisposed individuals who have never suffered with articular inflammation or uratic deposits, it is a common event to witness transient spasms of the fibres of the orbicular muscles of the eyes and mouth, or of the facial muscles and muscles of the extremities. Some observers are of the opinion that epileptiform convulsions may be occasionally excited by similar irritation of the brain and nervo-muscular apparatus with gouty blood. A further analogy with epilepsy is suggested by the fact that these spasmodic affections are occasionally followed, as sometimes happens after an epileptic seizure, by temporary paresis of the over-excited muscles.

Angio-neurotic œdema is not infrequent among the gouty, especially among females and neurotic patients. It often appears about the joints, and in the loose areolar tissue of the eyelids, lips, breasts, prepuce, and labia. The phenomena of swelling and pain are rapidly developed, and often subside or are transferred elsewhere as rapidly as they appeared. Sometimes the hands or the neck are visibly enlarged for hours at a time, without considerable pain other than a sensation of stiffness and clumsiness in the affected parts. The occurrence of these phenomena among the members of a gouty family, together with their frequent association with other arthritic manifestations of a decided character, and their relief by colchicum and alkalies, all combine to show their dependence upon the specific diathesis.

The connection between the above-indicated symptoms and morbid excitations of the sympathetic nervous system is so clearly apparent that it is evident that gouty phenomena are not limited to the cerebro-spinal nervous apparatus. The visceral plexuses and nerves are frequently the seat of painful disturbances that affect the functions of secretion and nutrition. It is in the abdominal and pelvic organs that some of the most distressing manifestations of ganglionic nervous disorder occur. Painful menstruation and ovarian tenderness are common experiences, even before the access of articular gout, or even in cases that never advance beyond prodromal stages of the diathetic disease. The walls of the stomach, intestines, bladder, and urethra are not infrequently the seat of obstinate suffering that is relieved only by anti-arthritic measures. In many instances these pains are migratory and transient, skipping rapidly from one part of the body to another; but they often remain fixed for considerable periods of time. A distinctly paroxysmal character can be, however, usually observed, and nocturnal exacerbations are of frequent occurrence. Sometimes the coincidence of these paroxysms with the varying alkalinity of the blood can be clearly determined. Fatigue of every kind, moral, intellectual, and physical, operates powerfully to aggravate the painful attacks, and they are greatly ameliorated by rest and proper food. Among neurotic dyspeptics who have inherited the arthritic diathesis this form of neuralgia is not uncommon, even though pronounced symptoms of gout have never been experienced. Eichhorst mentions it as a gastro-intestinal neurosis which he enumerates among the phenomena of diabetes. Other writers have vaguely noted it as a symptom of "lithæmia," but its connection with the sympathetic nervous system, and its dependence upon arthritism, have not been defined with sufficient clearness by the majority of writers. These visceral neuralgias are most frequently experienced during the changeable weather of the spring and

autumn months, and during the early heats of summer, in this respect conforming to the course of gout. They usually occur among constipated individuals who have reached middle or advanced life; but they sometimes are felt by the youthful members of gouty families. When the stomach is chiefly involved, the painful paroxysms commence when the organ is empty—toward noon, or in the latter portion of the afternoon, or during the night, generally after midnight—and they persist for one or two hours or until relieved by food or medication. The favorite seat of the pain when the stomach is principally affected is in the epigastrium or in the left hypochondrium. It is not limited to a single focus, but is vaguely diffused through the upper portion of the abdomen. Sometimes it extends into the cardiac area, or even as far as the arms. The character of the pain is of a nature that distinguishes it from other abdominal pains. It may be accompanied by tenderness of the epigastric region, particularly in the sternal third of the right rectus muscle, but such tenderness is distinct from gastralgia. It is not increased by pressure or by movement. The patient may cough, sneeze, laugh, walk, or run without influence upon the location, character, or intensity of the suffering. Ordinarily the paroxysm is not intolerable, but sometimes it is horribly severe, and is attended by a feeling of fearful exhaustion. It is a dull, deep-seated, widely diffused and persistent distress, quite different from ordinary gastralgia, colic, or peritonitis. It cannot be mistaken for the pain that exists in the gastric crisis of tabes dorsalis, or in chronic alcoholism, or in peripheral neuritis. By the sufferer it is readily distinguished from the more tolerable pains that occasionally have their seat in the abdominal wall, sometimes alternating with the gastro-enteralgic paroxysms. In short, it possesses all the characteristics of neuralgia affecting the sympathetic nerves. Such pain, when severe, is more intolerable than ordinary peripheral neuralgia. When the enteric plexuses are involved, the distress is usually less severe, but not less annoying than when the stomach alone is affected. Sometimes the pelvic nerves are the seat of irritation, and the patient may suffer intensely with rectal or vesical agony, especially after sexual intercourse. Prolonged and painful erections sometimes prevent sleep during the later hours of the night. During the intervals between the paroxysms, especially if food and sleep have been procured, bodily comfort may be complete. But the termination of gastric digestion, or the occurrence of bodily fatigue, or an exposure to cold damp air may be immediately followed by a return of pain. Gradually the patient becomes exhausted from suffering and loss of sleep; he is morbidly sensitive to cold, becomes neurasthenic, and is incapable of physical

or mental activity. Yet some of these sufferers present a florid appearance, and retain their usual weight. Many of them are hypochondriacal; and some of the more intelligent class can scarcely be persuaded that they are not victims of malignant disease of the stomach or other abdominal organs.

The Influence of Gout upon the Genito-Urinary Organs.

The gouty kidney has been already described, but it is impossible to insist too frequently upon the insidious manner in which an interstitial nephritis may be established under the influence of an excessive circulation of urates through the kidney. Not infrequently does this occur in cases of latent arthritism where no articular deposit or inflammation has ever happened. The only unusual symptom may be an increase in the urinary excretion, especially when, as during pregnancy, there is some hypertrophy of the heart. But the opposite condition may also obtain, with an enfeebled heart and scanty urine. Whenever there is complaint of headache that is unusually severe and persistent, or when there is debility and vague bodily distress without apparent cause, the condition of the kidneys should be carefully investigated. Under such circumstances the urine will often be found acid, depositing crystals of uric acid, and exhibiting a trace of albumin when treated with heat or nitric acid. So long as no unusual trial or effort disturbs the bodily functions, all these symptoms pass unnoticed, but any little disorder of digestion, a severe cold, the recurrent menstrual flux, or the occurrence of parturition, may arouse symptoms of intoxication that vary in severity from the ordinary forms of headache to convulsions and uræmic incidents of the most fatal character. It is in this insidious manner that many of the accidents of pregnancy and parturition are prepared among females who belong to gouty families, and who, perhaps, exhibit few other indications of an inherited predisposition.

The occurrence of renal congestion bears a certain distinct relation to articular gout. It is characterized by lancinating pain deep in the loins, and is sometimes accompanied by hæmaturia and a fugitive trace of albumin in the urine occurring alternately or coincidently with articular disease. These symptoms suggest the existence and passage of renal calculi, but they are often experienced when no discharge of gravel or calculus takes place. But since the discharge of such obstructive masses does not invariably occur at the time of the attack of renal colic, it is not always safe to conclude that every case of pain in the loins accompanied by hæmaturia without gravel or calculi is a case of renal gout. The close relation between gout and

gravel that unquestionably exists will be more fully discussed on a subsequent page.

The bladder is often affected during the course of gouty disorder. The symptoms of visceral irritation are more frequent among arthritic patients than among others. Irritation at the neck of the bladder, causing painful desire to urinate and accompanied with, or followed by, burning sensations along the whole length of the urethra, are the signs of this functional disturbance. The urine is of rather high specific gravity, clear, and acid. When the irritation advances to the stage of inflammation the urine is charged with mucus, leucocytes, and urates, forming a considerable milky-looking sediment as the liquid cools. Occasionally, there is hemorrhage from the lining of the bladder which cannot be ascribed to the presence of stone, or to villosities, malignant growths, or the other usual causes of bleeding in this locality. When coincident with neuralgic pains elsewhere that alternate with articular gout, such discharges are usually due to the diathetic disease, and are comparable to the attacks of nose-bleed with which so many youthful arthritics are familiar.

The prostate gland often suffers, and it is more liable to enlargement among the gouty than among other elderly people. The fact that such patients are prone to habitual constipation, hemorrhoids, gravel, and stone in the bladder, adds greatly to their chances for prostatic disease.

Gouty urethritis is not uncommon as a symptom that may appear toward the close of an arthritic attack. Among youthful arthritics it is sometimes excited by copulation independently of gonorrhœal infection; and it may occur spontaneously without sexual intercourse. In all such cases, however, the character of the urethral discharge should be determined by the aid of the microscope before deciding upon the absence of infective cocci. In certain cases thrombosis of the veins in the cavernous structures of the penis takes place, and the fibrous septa and sheath of the organ may become infiltrated at different points, causing chronic fibroid thickening that interferes with the free passage of the blood, and excites chordee and painful erections that are sometimes very persistent. Enlargement and induration of the testis may also exist. This gouty variety of orchitis is seldom as firm and dense as the other forms of testicular inflammation.

Uterine gout has been described by Sir James Simpson, but there is no satisfactory evidence of organic uterine disease that can be properly ascribed to gout. But there is abundant evidence of the fact that women who belong to gouty families are frequent sufferers with painful nervous sensations and disturbances of function involv-

ing the organs within the pelvis. Such patients suffer with leucorrhœa, dysmenorrhœa, uterine catarrh, herpetic eruptions about the vulva, and various erosions of the cervix, that either accompany or alternate with the eczema, bronchitis, asthma, and other arthritic affections that are so characteristic of the diathesis. They also have frequent experience of lumbar neuralgia, sciatica, hemorrhoids, pruritus of the vulva, and sudden violent determinations of the blood to the pelvic viscera. It is at the time of the menopause that these incidents are most frequent and most annoying. Attacks of metrorrhagia are not infrequent under such circumstances, and they often alternate with congestive paroxysms affecting the lungs, liver, and other viscera. In chronic cases such a degree of over-sensitiveness is developed that pain accompanies every movement of the abdominal and pelvic organs; and the neck of the uterus becomes intolerant of the slightest touch. The happy effect of warm baths and alkaline medication throws a clear light upon the nature of many of these cases, and points the way to relief that cannot be procured by topical treatment. Whenever vulvar pruritus cannot be explained by the existence of diabetes, leucorrhœa, uncleanliness, or the presence of parasites, it will generally be found that the patient belongs to a gouty family; and a careful inquiry will frequently result in the discovery of other slight and often disregarded evidences of the arthritic predisposition. If, therefore, uterine gout does not exist, it is certain that uterine disorders may be most profoundly influenced by the disease, even in its most obscure and latent form.

The Influence of Gout upon Diseases of the Skin.

From the remotest antiquity a connection between gout and certain cutaneous diseases has been remarked by all clinical observers who have seen much of the disorders that are experienced by the wealthier classes of society. It is true that authors who have based their opinions upon hospital and dispensary practice have denied, or sought to minimize, this connection. But this is so by reason of the fact that few among the pauper class are ever placed in circumstances favorable to the evolution of gout. They are usually the victims of starvation, exposure, dirt, tuberculosis, rheumatism, malaria, and syphilis; and they exhibit the skin diseases that are favored by the disorders of nutrition that are thus provoked. Similar cutaneous maladies may exist among those who are predisposed to gout; but careful observation reveals the fact that in that class of patients there is a conspicuous tendency to the manifestation of particular varieties of skin disease rather than the miscellaneous display that is apparent

among other classes of cutaneous sufferers. It is also observed that among the gouty, skin diseases are prone to alternate with articular attacks, so that certain utterly intractable and distressing eruptions disappear entirely during the course of an attack of gout in the feet or elsewhere. The alternate disappearance and return of eczema and gouty dyspepsia have been frequently noted by all the great clinical teachers from the days of Galen to the present time; so that the dependence of certain eruptions upon an arthritic condition may be considered a fact as well established as that of the connection between gout and interstitial nephritis, heart disease, bronchitis, asthma, or any others from the long list of maladies that are either dependent upon or modified by gout. All of these disorders may be initiated by other causes, but their course and duration are dependent not so much upon the exciting cause as upon the condition of the tissues that are excited.

Without stopping to consider the ulcerations of the skin that may be produced by the enlargement and pressure of tophi, we may enumerate the cutaneous diseases that are most frequent among the gouty. They are eczema, impetigo, acne, pityriasis, psoriasis, urticaria, lichen, and prurigo.

Eczema is frequently witnessed among the children of gouty families. It appears upon the face and scalp, and other parts of the body, and does not differ essentially from the eczemas that occur among other children, unless it be in the greater obstinacy with which it rebels against all treatment. It is sometimes dry and indolent, while in other cases it assumes the moist and acutely inflammatory type. At about the age of twenty-five years, it begins again to torment the future arthritic subject, appearing usually upon the lateral surfaces of the thumb, index, and middle finger. The eruption is seldom moist and does not cause much annoyance from itching; it is a dry eczema that causes superficial desquamation of the cuticle, and but little else in the way of inconvenience. The spring of the year is the favorite time for its manifestation, and it gradually disappears during the summer, to be renewed again the following year. Similar manifestations occur in circumscribed patches over the sternum, in the axillæ, genito-crural folds, at the flexures of the elbow and knee-joints, and around the ankles. These eruptions are usually dry and scaly, and they often itch beyond all endurance. With advancing years and increasing corpulence, they may assume the form of intertrigo wherever they occupy the opposing folds of the skin, such as exist under the breasts, in the groins, and between the prepuce and the glans penis.

Impetigo is not uncommon among the children of the gouty. It

does not differ from the similar manifestations that occur among unhealthy infants.

Acne occurs at and after the age of puberty. It is usually more severe and obstinate among the future gouty than among other subjects, and it tends to assume an indolent form with large, violaceous pustules that exceedingly disfigure the countenance, and leave permanent scars upon the cheeks, temples, and nose.

Psoriasis presents no special peculiarities among the gouty, except that it may disappear during articular attacks, thus showing the tendency to alternation that is characteristic of other disorders that are more or less dependent upon arthritism.

Lichen and prurigo are very common among elderly people who belong to the arthritic class. The cutaneous manifestations are not conspicuous, but there is an intolerable itching that is out of all proportion to the visible appearances, indicating the largely nervous character of the affection. The suffering is more or less paroxysmal, and is often worse at night, or after fatigue of mind or body, or when the bowels are confined. Such patients procure temporary relief by scratching, so that their skin is often more deeply marked by the nails than by the eruption. They are intolerant of cold and heat, and cannot enjoy tub-baths on account of the fearful burning and itching all over the body that are excited by sudden change of temperature affecting the cutaneous surface. The region around the anus is often among old people the seat of pruritus that is exceedingly persistent and tormenting.

Furuncles and carbuncles frequently precede or alternate with attacks of gout. They are prone to follow one another in successive crops for a considerable period, perhaps until an arthritic inflammation clears the body for a time. In all such cases, however, there should be careful examination of the urine for sugar, since the existence of diabetes is a common cause of furuncular eruptions.

In all these cutaneous disorders, however, there is nothing pathognomonic. Their relation with gout must be determined by their concurrence or alternation with articular symptoms, and by the history of the patient rather than by any special peculiarity of the eruptions themselves. The arthritic condition of the patient is not necessarily the cause of the skin disease, but it favors its appearance and gives color to its manifestations. In certain cases an excess of urates can be detected in the liquids that are discharged from the weeping surface of an eczematous patch, for example; and one is tempted in view of such incidents to explain the eczema by assuming a morbid action of the urates upon the cutaneous tissues. But in other cases, there is an absence of urates from the eczematous discharge and from

the blood itself. An excess of uric acid alone cannot, therefore, be the only cause of the lesion, though it must undoubtedly aggravate the disease when it is present. This aspect of the subject will be more fully discussed in connection with the pathology of gout, in a subsequent section.

Manifestations of Gout in the Organs of Special Sense.

Disorders of the eye are not infrequently encountered in gout similar to those seen in rheumatism. Many authors have failed to distinguish clearly between them for the reason that their symptoms are nearly identical, though their causes may differ. There are also diseases of the eye occurring in gouty subjects that are only indirectly due to arthritism. Thus a gouty patient may have black specks floating in the field of vision, or may seem to be looking through a fog, or he may be embarrassed by central scotomata. He may even become suddenly blind; and, on ophthalmoscopic examination, a retinal hemorrhage may be discovered. This is due to the state of arterial disease that accompanies interstitial nephritis, so that gout is not the direct cause of these visual accidents, but is their remote antecedent. In like manner it may be the indirect and remote cause of certain cases of arcus senilis, atrophy of the optic nerve, and progressive loss of sight in elderly patients who have suffered long with chronic gout. Yet other elderly subjects who have never had experience of gout may be afflicted in the same way, illustrating the well-known pathological fact that very similar diseases may be excited by widely different causes.

Among the disorders of the eye that are directly connected with acute gout may be mentioned a variety of conjunctivitis that frequently precedes an articular inflammation. It sometimes so far antedates the attack that it must be reckoned among the prodromal symptoms; in other cases it accompanies the onset of the pain and swelling in the joint. It is characterized by an abrupt and apparently causeless beginning; there is considerable pain, redness and swelling of the conjunctiva, usually without much photophobia, and a rather copious watery discharge. So soon as the joint becomes inflamed, these symptoms all subside, and disappear in the course of twenty-four hours. The earlier attacks leave no trace; but if often repeated, the sclerotic vessels become permanently dilated, and a chronic blepharitis may be established.

Garrod and others have observed, in a number of instances, the formation of genuine tophi in the conjunctiva and sclerotic coat of the eye. These rare deposits are not found during the acute attacks

of gout, but are usually the result of gradual and unnoticed infiltration.

In like manner, inflammatory attacks affecting the eye are more common during the course of irregular gout than in acute forms of the disease. They occur, like other erratic manifestations, with an abrupt commencement, a rather violent course, and a sudden termination whenever articular or visceral crises begin. They usually involve the iris and the choroid, and sometimes invade the sclerotic. When this coat is inflamed an injected zone is visible through the transparent conjunctiva, more conspicuous than elsewhere around the insertions of the ocular muscles.

Iritis and irido-choroiditis are more frequent than sclerotitis; they are, in fact, the most common of the gouty inflammations of the eye. They are usually encountered among the members of arthritic families, who have gouty deposits in the joints, ears, and elsewhere; they are liable to periodical recurrence, especially in the spring of the year, like regular articular gout; they frequently occur independently of other manifestations, but sometimes they follow the outbreak of inflammation in the joints. Despite the efforts of eminent ophthalmologists to distinguish the gouty iritis from other varieties of the disease, no such distinction can be made. There are no pathognomonic symptoms, and from the clinical point of view there is no difference between arthritic iritis and the varieties of the malady that are excited by rheumatism or syphilis. But in the gouty forms of iritis there is a greater tendency to paroxysmal exacerbation of the symptoms, as the disease progresses by fits and starts. These exacerbations are accompanied by serous and fibrinous exudations that greatly increase the liability to posterior synechia with all its train of deleterious consequences.

Another peculiarity of gouty irido-choroiditis is its tendency to recurrence, and its final production of complete glaucoma in many instances. It is also singularly intractable to ordinary methods of medication, often yielding only to treatment that is addressed to the underlying predisposition. In this respect the local lesions bear the same relation to gout that the lesions of luetic iritis hold toward syphilis. In each instance specific treatment is essential to a successful result.

The close relationship that exists between gout and rheumatism is nowhere more apparent than in the course of these ocular inflammations. Their symptoms, behavior, and results are clinically indistinguishable, whether excited by one or by the other of these diathetic disorders. Unless we possess a sufficient family record, or a personal history of articular or rheumatic accidents,

it will be often impossible to decide between gouty iritis and its rheumatic twin.

Gouty affections of the external ear have been already fully described in the section on morbid anatomy. The development of tophi in the body of the helix and at the other points of election goes on insidiously, without attracting any attention in the majority of cases. Sometimes, however, there are brief inflammatory attacks involving the external parts, causing great pain for a short time, but speedily subsiding as the disease develops elsewhere in the joints. It is usual to encounter progressive deafness among the gouty, as they advance in years. But it is a rare thing to find after death any evidence of uratic deposit about the articulations of the ossicles of the ear. The drum membrane becomes thickened, and the joints of the osseous chain in the middle ear become anchylosed; but even Garrod, with all his vast experience, was unable to find any appearance of tophaceous deposit. The loss of hearing progresses slowly, and without pain or noise in the ears. The membrana tympani grows thicker and less responsive to aerial vibrations; it often exhibits calcareous deposits in its layers, and the handle of the malleolus is no longer visible through it. Ankylosis of the stapes is of frequent occurrence, exercising a profoundly deleterious influence upon the auditory function by interference with the transmission of vibrations through the membrane of the fenestra ovalis to the fluids within the inner ear. These changes usually progress without pain, and they are not interrupted by inflammatory paroxysms of an acute character; so that the only evidence of gouty action in the middle and inner ear is to be found in the results of chronic inflammation and ankylosis in the chain of communication between the external and inner chambers of the auditory apparatus.

The Morbid Affinities of Gout.

In this lengthy enumeration of disorders and symptoms that are directly or indirectly connected with the manifestation of articular gout, it is often difficult to decide whether a particular malady is directly caused by the arthritic constitution of the patient, or is merely an accidental concomitant of the primary affection. It becomes also a matter of importance to ascertain the character of the tendencies, if any, that may be transmissible from generation to generation along a line of gouty descent. The influence of arthritism upon intercurrent diseases of a non-arthritic character demands careful study; as well as the reciprocal influence of such diseases upon the tendency to gouty manifestations of every kind. We have already noted the

frequent concurrence of asthma, bronchitis, heart disease, biliary disorders, gall stones, renal inflammation, gravel, and renal calculi with gout. A more detailed examination of this relationship will be found useful, not only for the purpose of discovering an answer to the questions thus raised, but also with a view to the acquisition of general ideas regarding subjects that have been too much neglected in the study of pathological anatomy; a study which has given precision to our knowledge of the topographical and histological features of disease without adding to the stock of ideas anything but notions regarding the local manifestations of disorder, and the local causes of morbid change. A broader view of the connection and relation of disease with constitutional conditions is needful for the complete comprehension of diathetic disorders like gout and the other members of the class to which it belongs.

Notable among the maladies that are most frequently associated with gout are the different varieties of lithiasis. Of these, biliary lithiasis is the most frequent and most evidently affiliated with gout. Of common occurrence among women and elderly men as a consequence of inactive habits and retarded nutrition, its existence among the gouty and in gouty families is still more often observed than among a corresponding number of patients who are not thus related. Hepatic colic, and the obstructions which are its cause, are more often encountered among women than among men, so that at first sight it might be inferred that, as the female sex is comparatively free from gout, biliary concretions are less favored by the arthritic predisposition than by its absence. But further investigation reveals the interesting fact that in the line of descent from a gouty ancestry it is usual for the men to experience articular disease, while their sisters escape inflammation of the joints, but suffer severely from other diathetic disorders. Among these, hepatic colic and biliary lithiasis are conspicuous. In a valuable work on the subject ("Traité des Coliques hépatiques"), Sénac has collected 166 cases of which 69 belonged to gouty families. Of these 69 patients 30 were themselves victims of gout as well as of lithiasis. Besides these 30 there were 26 more who had suffered from gout without belonging to arthritic families. Fifty-six of the whole number of lithiasics, therefore, were themselves gouty, while 95 (57 per cent.) were either gouty or belonged to a gouty stock. Of the remaining 43 per cent. it is probable that longer observation would have assigned a considerable number to the list of gouty subjects. Similar statistics have been furnished by other competent observers. Thus Bouchard found that of 100 cases of biliary lithiasis under his observation, 30 per cent. had gout among their hereditary antecedents.

Two facts serve to obscure in some degree this affiliation between the hepatic disorder and its articular relative: the sex of the patients, and their comparative youth. It has been already noted that women are less subject to gout than men. This may be explained by their greater temperance, and by the influence of menstruation. Lithiasis, moreover, is a disorder in which the painful paroxysms of colic are most frequent in early life. Young women, therefore, may suffer with biliary colic long before they become gouty, if ever; so that their predisposition to arthritic disease may for a considerable time, or forever, escape notice. In certain cases, however, as time advances, the attacks of colic become less frequent and less severe, and the patient begins to exhibit either the genuine crises of articular gout or other of the minor manifestations of the diathesis, such as chronic thickening of the joints of the fingers and toes, or Heberden's nodes may appear upon the distal articulations of the phalanges. Occasionally, after the establishment of articular gout, it happens that its crises alternate with the attacks of colic, affording a complete demonstration of the close relationship that exists between the two disorders. All that has been noted regarding the affiliation of biliary lithiasis and gout is equally true of renal lithiasis. The clinical teachers from the most remote antiquity to the present time are all agreed upon this observation. Whether manifested in the form of stone in the bladder, gravel, sand, or renal calculi, the relationship is equally evident. Usually, the occurrence of gravel antedates the articular disease; but sometimes it follows its attacks, or alternates with them. Occasionally, but rarely, the two maladies are coincident, and the patient suffers with renal colic at the same time that he experiences pain and swelling in his joints. Sénac, who enjoyed unusual opportunities for observation among patients who resorted to the springs at Vichy, remarked the fact that of 166 cases of biliary calculi, 98 had suffered with gravel, and 95 had either experienced gout in their own persons or were descended from gouty ancestors. In three instances urinary calculi were also present, an unusually large proportion, since the percentage of such calculi among all kinds of patients is less than one per cent.

It is an interesting fact that visceral calculi when encountered in gouty subjects are not necessarily composed of uric acid alone. They are sometimes made up of ammonium urate, or of calcium oxalate. These last may be, however, considered as derivatives of uric acid, since that substance can be split up into urea, allantoin, and oxalic acid. Sometimes the growth of a stone in the bladder is modified by changes in the composition of the urine, so that the irregularly spherical mass comes to be formed of concentric layers of

different substances deposited around the original nucleus. Thus a stone may consist of alternate layers of calcium oxalate and uric acid; or numerous calculi may be successively formed of earthy phosphates, urates, and pure uric acid. Sometimes the urine exhibits a varied succession of earthy sediments which continue to appear until everything is cleared up by a pronounced attack of articular gout.

An intimate connection between gout and diabetes has long been remarked. The two disorders are often encountered along the same line of descent, and not infrequently they are experienced by the same individual. It is usually among those who have had early attacks of gout, or who have arrived at middle life and have acquired the arthritic constitution, that this form of diabetes is evolved. The patients are big, stout, and florid, great eaters, and of inactive habits. They may have suffered with acid dyspepsia or with biliary or renal lithiasis. At first they complain of inexplicable lassitude, and of profuse sweating on slight exertion, yet they do not lose weight or color. After a time an inordinate thirst attracts the attention of every one, and an examination of the urine reveals the presence of sugar. In many instances such an attack of glycosuria is merely a transient incident that soon yields under the influence of a change of diet and appropriate medication. The patient recovers his vigor, and his health appears to be quite restored. But in the majority of cases this glycosuria, though temporary and fugitive, is an indication of impending disaster. It proves that the liver is no longer competent to guard the system at all times against the excessive introduction of sugar into the general circulation. Unless the diet and habits of the patient are carefully regulated, there will be, sooner or later, a transition from simple glycosuria to confirmed diabetes.

As a general thing, however, the course of gouty diabetes is slow and comparatively mild. It is often witnessed among the corpulent of both sexes. It often appears among women who have led a life of leisure, and have gained in weight with advancing years. At the time of the menopause they frequently begin to exhibit phalangeal nodosities, or other arthritic symptoms, and their urine contains sugar. They often suffer with vague nervous symptoms, are afflicted with sleeplessness, and are exceedingly prone to attacks of vulvar pruritus. In this condition, if prudent in the matter of diet and mode of life, they may pass many years without marked failure of health; but usually the glycosuric crises become more frequent and persistent, until at last the symptoms of confirmed diabetes are established. When this stage has been reached the course of the disease does not differ from that of the ordinary forms of diabetes.

and the patient inevitably succumbs to the exhaustion incident upon gangrene, pyæmia, inanition, or tuberculosis. To express in statistical form the relationship between gout and diabetes is a difficult matter. The physician who studies these diseases in a wealthy clientage, or at the mineral springs where arthritic patients congregate, will arrive at results that differ from the opinions of observers whose knowledge is principally derived from the observation of paupers in a public hospital or dispensary. Thus Seegen, at Carlsbad, found that 30 per cent. of his diabetic patients were also gouty; while Griesinger, at Berlin, could discover but three gouty subjects among 225 diabetics. At Vichy, Durand-Fardel, excluding all cases of biliary lithiasis, found, among 270 cases of diabetes, that about 14 per cent. were gouty or sufferers with gravel. Gout and diabetes are often associated in the same line of family descent, but they seldom attack the same individual. The following table, from Bouchard, indicates the close affinity between diabetes and other arthritic disorders that becomes apparent when the family history of the patient is subjected to scrutiny. In the families of 100 diabetics he found:

Rheumatism	54
Obesity	36
Diabetes	25
Gravel	21
Asthma	11
Eczema	11
Hemicrania	7
Biliary lithiasis	7

Since all these diseases have been shown to be most intimately connected with the arthritic diathesis, it is difficult to resist the belief that they are all connected with a common cause. Their alternation with each other has been often observed; and their general disappearance, for a time at least, after an acute attack of gout serves to emphasize their apparent kinship.

Obesity is another morbid condition that is closely affiliated with gout. Though seldom manifested together in the same person, the two disorders are intimately associated in the same families. Obesity is not uncommon among the children of gouty parents; and, conversely, gout is no rarity among the offspring of obese progenitors. Excessive corpulence is by no means the simple consequence of over-eating. It often persists in spite of modification of the diet, and is dependent upon deep-seated errors of nutrition that are peculiar to certain constitutions. It is usually associated with rheumatism, gout, asthma, gravel, diabetes, cardiac disease, stone in the bladder,

biliary lithiasis, or eczema—thus forming a component of that group of diseases with which gout is so closely connected. Of the cases gathered by Bouchard nearly one-half exhibited obesity as an hereditary disease, and gout was present among the relatives of one-third of the patients, while the other latent manifestations of arthritism occurred in the families of about half the number.

The connection between gout and rheumatism has been discussed at great length by numerous competent observers, but without arrival at complete unanimity of belief. These differences of opinion are largely dependent upon the manner in which the subject is approached. Regarding it from the clinical standpoint alone it is difficult to distinguish in every instance between the two diseases. But the pathological anatomy of gout differs widely from that of rheumatism, which chiefly manifests itself in the substance of the bones, and in a velvety splitting-up of the articular cartilages, widely different from the uratic infiltration of those structures. Rheumatism also attacks young children and other patients of every age, and is located as a poly-arthritis in numerous large joints; while gout is a disease of middle and later life, usually manifesting itself in but one joint at a time, and invading by preference the smaller joints of the feet and hands. Repeated attacks of rheumatism may visit the same joints without producing any permanent change in their structure; but it is an uncommon event for gout to leave an articulation without lasting evidence of its occupation. The value of these differential characteristics is somewhat minimized by Haig and others who do not consider gout and rheumatism as essentially different from each other. Regarding both diseases as chiefly dependent upon the retention of urates in the tissues, and their sudden discharge into the blood by reason of causes that occasion a reduction of the alkalinity of the circulating fluids, Haig expresses the opinion ("Uric Acid as a Factor in the Causation of Disease," 1894) that the greater relative vascularity and alkalinity of the joints in young people protects them from permanent incrustation and infiltration with uric-acid compounds. The kidneys of such patients, also, are more efficient in earlier life than in later years; consequently the elimination of urates in rheumatic attacks will be so complete that no trace can remain behind. This fact is sometimes witnessed in acute articular gout. But with advancing years the eliminating organs become less competent for their task, the joints become less vascular and less alkaline, so that urates are freely and permanently deposited in their substance, exciting all the phenomena of chronic gout. According to this line of reasoning uric acid and its nitrogenous congeners

are the principal causes of both gout and rheumatism; while the differences that undoubtedly exist are chiefly dependent upon the relative adequacy and activity of the eliminative organs in different subjects.

Without proceeding further at present with the discussion of this feature of the subject, it is impossible to deny the intimacy of the affiliation between rheumatism and the group of diseases in which gout is so conspicuous. Fuller has shown that of 300 rheumatic patients, whose antecedents he had investigated, about one-third (96) had rheumatic ancestors; while nearly one-half of his gouty patients were of similar descent. Of Bouchard's 100 gouty cases 25 had rheumatic relatives behind them. The same author has recorded 39 cases of rheumatism in the families of 100 patients suffering with biliary lithiasis, and 28 of them had also experience of rheumatism in their own persons. In like manner, he found 35 cases of rheumatism in the families of 100 cases of obesity; and 45 cases similarly related to 100 diabetic patients. It is hardly possible to give a clearer proof of the intimate connection that exists between all of these diseases.

The question of the pathological affinities of the so-called Heberden's nodes has been often discussed. Appearing upon the dorso-lateral surface of the two distal articulations of the fingers, they usually develop slowly upon either side of the median line, and produce considerable deformity of the joints. Sometimes they grow without exciting much pain, but in many cases their appearance is preceded and accompanied by severe suffering and articular swelling in the affected parts. They contain no mineral constituents, but are made up chiefly of fibrous tissue that is formed under the influence of chronic inflammation, often involving also the joints and the ends of the bones themselves. In all these particulars these little tumors are allied with chronic rheumatism; but in many other respects they seem to be related with gout. The English authors, with their large experience, generally incline in favor of the gouty character of these growths. They are very seldom associated with acute rheumatism. They commonly occur among elderly women after the menopause, and especially among women who belong to the luxurious class, and who number among their relatives a considerable proportion of gouty subjects. The absence of tophi does not decide against the gouty kinship of these tumors, for women are less liable than men to such incrustations, and many cases of articular gout escape for a long period without notable infiltration of the joints. The frequent existence of these nodes upon the fingers of patients who suffer with asthma, sciatica, neuralgia, hemicrania, and other manifestations of

the arthritic diathesis, forms another argument in favor of their gouty relationship.

Similar questions have been raised regarding the affinities between gout and arthritis deformans. By many pathologists this has been regarded as a strictly rheumatic affection; others have described it as a malady that partakes of the nature of gout; while a third class of writers look upon it as an independent disease, exhibiting certain features of resemblance with both gout and chronic rheumatism, but originated by entirely different causes. In order to indicate its clinical relationship, it is frequently described by English authors as rheumatic gout. But aside from the fact that it is usually manifested in the smaller joints of the extremities, and that it may produce deviations and deformities of the fingers that closely resemble the ulnar deviation of the fingers that is sometimes occasioned by chronic gout, the points of resemblance are not very numerous. It is generally witnessed among broken-down old people, specially those of the female sex, who have been subjected to poverty, hardship, cold, and damp. Tuberculosis and chronic nephritis are also often noted among its antecedents or concomitants. The diseases so frequently affiliated with gout—diabetes, obesity, lithiasis, etc.—are rarely encountered in the environment of arthritis deformans. Still it is not uncommon to find rheumatism among the relatives of these patients, and gout among their ancestors. The three diseases probably originate in a common predisposition, but their different modes of evolution depend upon the conditions of life, diet, exercise, exposure, occupation, etc., that vary according to the residence and the social rank of the individual.

The Hereditary Consequences of Gout.

Very little accurate knowledge has been acquired regarding the remote consequences of gout that are manifested along the family line of descent. We have seen that the disease itself often reappears in one generation after another; and its immediately related diseases exhibit the same tendency. But the questions continually arise,—Are there other diseases which are more likely to attack the descendants of a gouty ancestry than to be manifested among those who are not thus weighted in the struggle for existence? Is there any antagonism between gout and other maladies?

It has been long believed that gout favors the development of carcinoma, and that cancer might be regarded almost as the terminal stage of arthritism. But those who suffer from genuine gout seldom die of cancer. If in any way directly connected, it must be either

though the affiliated diseases, or by descent. In neither of these directions has it been possible to arrive at anything like probability. The two diseases are not apparently related, nor are they antagonistic.

Tuberculosis is rare among the gouty—its parasite cannot easily find lodgment in the tissues of the well-fed arthritic. Possibly the excess of acid in the fluids of the gouty subject is sufficient to antagonize the growth of the bacillus. But among the descendants of gouty parents tubercular disease is not an uncommon event. It is difficult to prove this assertion by statistics, for they have not yet reached this aspect of the subject. But among the great clinical observers there prevails a very decided belief in the fact that tuberculosis often appears among the children and descendants of arthritic parents. Some have estimated that one-quarter of their consumptive patients belong to such families. The explanation of these facts is to be sought in the different conditions of life to which successive generations are subjected by the occurrence of disease. Gouty parents exhaust their vitality and their substance in good living and inactive occupations. Their children and their children's children may be thus both physically and financially placed in the decadent class. It is upon such people that the tubercular parasite is liable to fix itself; and in this way the enfeebled offspring of men who have filled a conspicuous place in society, finding themselves unable to continue in the enjoyments and comforts of life that fell to the lot of their progenitors, fall an easy prey to the diseases of degeneration. As prodigality begets poverty, so does gout bring forth tuberculosis.

As some slight compensation for this result it is interesting to learn that the course of tuberculosis in these subjects is less rapid and virulent than in ordinary cases. The disease progresses by fits and starts, in a sort of paroxysmal fashion, with considerable intervals between the successive attacks. In this way is developed the long-continued form of pulmonary consumption that persists for years without seriously undermining the health and strength of the individual. In these cases the tendency to cicatrization and to calcification of the pulmonary deposits is highly characteristic. The effort toward natural recovery is continually apparent, and it is aided by the very measures that favor the evolution of the gouty predisposition. In many instances the appearance of arthritic phenomena is followed by an at least temporary subsidence of tubercular manifestations.

Functional nervous diseases are of exceedingly common occurrence among the descendants of gouty families—especially among the female members of such families. It is not alone the enfeeblement of the constitution consequent upon arthritism that produces

such irritable weakness of the nervous system, for the offspring of a tuberculous stock, though debilitated and anæmic, rarely exhibit any special proclivity to the neuroses. The researches of Haig have made clear the irritant effects of uric-acid compounds when present in the circulating fluids. They excite the vasomotor nerves, thus interfering with the regular movement of the blood through the arterioles, and they disturb the sensory organs to a painful degree. As a consequence of these disorders, the nutrition of the tissues is retarded, and the nervous apparatus becomes weakened and over-sensitive. Hence the frequent incidence of every variety of neuralgia among the gouty and their descendants. Including rheumatism and the other allied diseases under the arthritic class, we find that a large proportion of the neuroses have their origin in the arthritic predisposition. Grasset has long since called attention to the fact that such neuroses as cannot be referred to syphilitic or malarial causes are usually dependent upon gout or rheumatism. Charcot and his pupils have repeatedly verified this observation. Among elderly people who suffer with chronic nitrogenous poisoning a functional form of amnesic aphasia is very common. It is characterized by a defect of memory relating chiefly to the names of persons and things, and is not accompanied by motor paralysis. The patient loses confidence in himself, and often feels oppressed with the feeling that he has forgotten something, or has failed in the performance of some duty. All these symptoms yield rapidly to treatment by elimination with colchicum and sodium salicylate—especially if at the same time a meat diet be excluded.

Mania and melancholia are not infrequent consequences of cerebral degradation among gouty descendants; but it is difficult to assign its true value to simple arthritism in such cases, for their causes are so frequently complicated with the effects of alcoholism, syphilis, tuberculosis, and poverty, that it is impossible to traverse the tangled web with any satisfactory success. Intense depression of spirits is a common incident in deficient elimination of urates. The connection between gout and epilepsy among the descendants is hardly doubtful in many cases. It is also a well-known fact that epilepsy of an incurable type may be greatly benefited by treatment that is calculated to prevent the accumulation of urates in the system. It is highly probable that the advantages attendant upon long courses of potassium iodide associated with the bromides is largely due to the good effect of that salt in cases of chronic arthritism.

Exophthalmic goitre is another of the neurotic affections that seem to be often dependent upon gouty antecedents of an hereditary character. In like manner the milder forms of hysteria, nervousness,

spinal irritation, and neurasthenia with its protean manifestations, are frequently encountered among the descendants of gouty families. Such patients are often delicately constituted, and live the most exemplary lives, so that a prolonged investigation may be necessary before it can be determined that their neurotic constitution and nervous temperament are the results of ancestral gout. Yet this discovery will often reward a carefully conducted inquiry.

The Relations between Gout and Other Intercurrent Diseases.

Numerous authors have remarked that certain diseases are attended by great mortality when they occur in gouty patients. Thus Murchison has affirmed that typhus fever in a gouty subject is inevitably fatal. Schmidtmann utters the same opinion regarding low forms of fever in general. Erysipelas has also been included in the same category. Sir Spencer Wells has observed that among the gouty, syphilis tends to assume a scorbutic form. Pregnancy, in the case of a gouty woman, is liable to be attended with unusual difficulties, and may be terminated by abortion.

Now with regard to all these intercurrent disorders, the danger arises not so much from the specific diathesis of the patient as from the fact that his or her internal organs are not in a healthy condition at the time of invasion by an intercurrent disease. The authors above mentioned have in several instances made special note of the fact that the kidneys or other organs were in a state of chronic inflammation and degeneration. Many of the cases, such as typhus fever and erysipelas, were examples of infectious disease. It is well known that the prognosis in such diseases, as also in pregnancy, is determined largely by the eliminative adequacy of the kidneys and the competency of the heart. If the heart can retain vigor sufficient for the task of maintaining the circulation, and if the kidneys can free the system from the flood of toxins and excrementitious substances that are poured into the blood during the course of a fever, recovery will be reached at last. But if the heart and kidneys fail, the patient must inevitably succumb. Now in advanced cases of gout those organs are seldom healthy. Chronic nephritis and chronic myocarditis are slowly undermining the constitution; and when an intercurrent disease adds to the burdens of a patient who is scarcely able to support the task of ordinary living, he can no longer maintain himself, and death ensues as a consequence of uræmia and heart failure. But in mild cases of a gouty predisposition, where the vital organs are still practically intact, an intercurrent disease need not be inevitably fatal. In fact,

it has been already noted that the progress of tuberculosis is often delayed and rendered more tolerable by the concurrence of gouty tendencies.

As to the effect of intercurrent diseases upon the crises of gout, information is almost entirely lacking. Cases have been recorded in which pneumonia, or pleurisy, or tonsillitis, has been averted by an attack of gout. But it is probable that these were congestive paroxysms preliminary to the articular crisis, and that they were to be regarded as premonitory symptoms of the principal disease, rather than as independent maladies arrested by the appearance of gout. Still, it is not impossible that an independent disorder which would not usually lead to any result beyond its own evolution may, in an arthritic subject, awaken the latent predisposition, and precipitate a crisis, just as the same thing is often effected by fatigue, worry, or bodily injury. Whatever tends to hinder the processes of elimination may become the exciting cause of an attack of gout. Thus it is not uncommon to witness an explosion of articular inflammation after trifling contusions or sprains. The tissues composing the injured joint become less alkaline as a consequence of excessive use or injury, and urates are at once deposited in them, giving to the affection a specific character and an intensity that would not have been manifested but for the existing predisposition. Sir James Paget and other surgical teachers have contributed numerous observations of this nature. It has been also frequently remarked that limbs and joints that have been weakened by previous disease or injury are more likely than other parts of the body to be attacked with gout or rheumatism. In this respect these two kindred maladies closely resemble each other. An old sprain is liable to become the seat of either rheumatism or gout, according to the individual predisposition of the patient. For example, a young man of my early acquaintance one day injured his knee by falling over a log while hunting. He was confined to his bed for several weeks with ordinary inflammation. Three years later, inflammatory rheumatism attacked the weakened knee, and extended to the other. In advanced life gouty inflammation appeared first in the knee, and then in the classical situation upon the great toe of the affected limb, while small uratic deposits invaded the ear and the fingers. Sir A. Garrod has recorded the history of a case in which the onset of acute gout appeared to have been determined by the shock of an injury. A man had several ribs broken by a blow from the pole of a wagon. Almost immediately he began to experience pain in his elbow, followed by swelling of the fingers of the corresponding hand. This extended on the next day to the opposite knee and to the foot. The case was considered to be one of

rheumatism, but its severity and its extension to the smaller joints awakened a suspicion of gout, which was verified by the discovery of uric acid crystals in the serum of the blood. Subsequent inquiry developed the fact that the patient belonged to a gouty family, and that he had suffered an attack in the great toe some fifteen months before the present injury.

The exalted sensitiveness of the tissues in cases of a predisposition to gout is often so great that the slightest injuries may suffice to disturb the balance of health and to induce an acute attack. Sir Dyce Duckworth has collected a number of illustrative examples. Thus an outbreak has been known to follow the bite of a gnat, or the pulling of a tooth, or the scratch of vaccination, or the letting of blood from a vein. Operations upon the eye and other minor surgical operations have thus sufficed to excite the manifestations of the disease. In like manner certain natural morbid disturbances may arouse the latent predisposition. Thus a copious discharge of blood from the nose has been followed by gout; but in such cases there is room for the opinion that the hemorrhagic flux was really one of the prodromal symptoms of the articular inflammation. In one instance, at least, I have seen passive hemorrhage from the lungs precede a gouty attack in a patient who never was tuberculous. Charcot has recorded the case of a hemiplegic woman whose paralyzed limbs were attacked with gout, infiltrating the joints with uratic deposits, while the non-paralyzed side remained healthy throughout life.

The similar effect of intercurrent diseases and injuries in exciting either gout or rheumatism, according to the predisposition of the individual, affords another interesting proof of the close relationship that exists between the two diseases. Courty, of Montpellier, has reported a number of cases in which the operation of lithotrity was followed by rheumatism in certain instances, and by well-marked gout with uratic deposits in others. Such facts serve to illustrate the modifying influence of constitutional conditions under the operation of identical excitants.

It can hardly be affirmed that gout exercises any particularly unfavorable influence upon the healing process in open wounds, or in fractures of the bones. Many gouty subjects ordinarily enjoy vigorous health, and their injuries heal as readily as those of non-arthritic patients. But in old and cachectic cases, when the kidneys, the heart, and the liver have been long diseased, it often happens that wounds heal slowly and imperfectly. Before the days of antiseptic surgery this fact was probably more conspicuous than it is at present. The oculists were of the opinion that operations upon the eyes of the gouty were less successful than they were in other cases by reason of

a greater proclivity to inflammation among arthritic patients. Sir James Paget has emphasized the opinion that in the majority of chronic periosteal inflammations caused by traumatism, and of persistent cases of iritis, or of urethritis degenerating into permanent gleet, when the disease lingers interminably, like the obstinate forms of senile bronchitis which tend to become perpetual, gout is to be looked for as the determining cause of such intractability in the majority of cases from which the intervention of tuberculosis has been excluded.

An increased sensibility to pain after injury has been often remarked among the gouty. Thus light contusions excite a degree of pain that is out of proportion with the character of the traumatism. Ordinary neuralgias assume an inordinate intensity, and they sometimes persist for a long time after the apparent recovery of the injured tissues. I have seen this illustrated by the occurrence of excessive pain after the ordinary operations of surgery. In a gouty patient whose arm had been amputated at the junction of the middle and upper thirds of the humerus, there were recurring attacks of pain in the neck and shoulder, accompanied by spasmodic contractions of the pectoral muscles, which always yielded to the eliminative treatment with sodium salicylate and colchicum following a mercurial cathartic, and non-nitrogenous diet. Severe attacks of trifacial neuralgia occurring in plethoric subjects who were arthritically disposed I have known to yield under similar management. It is probable that in all such cases the local lesions are comparatively insignificant, but the irritability of the affected nervous tissue is exaggerated by the peculiar form of malnutrition to which it had been long subjected before the experience of traumatism revealed the heightened susceptibility of the sensory organs. In this way also may be explained the horrible intensity of the pain that characterizes gouty inflammation of the joints—so far exceeding the pain that is experienced in ordinary forms of arthritis.

Etiology.

From the review of the long array of facts thus set forth it is evident that gout is the most conspicuous manifestation of a peculiarly disordered condition of the constitution; a disorder that especially involves the processes of nutrition and elimination. Before proceeding to a further discussion of the nature of this departure from the normal standard of health, it is necessary to consider the conditions of environment, heredity, individual constitution, and acquired vice that promote such morbid variation. For it requires no very extended observation to perceive the fact that gout is not a universal disease,

but that it is peculiar to certain countries, to certain races, and to particular individuals among those chosen people.

Geographical Distribution of Gout.

In his "Handbuch der Historisch-geographischen Pathologie," Hirsch has shown that gout is chiefly encountered in the cities of the temperate zones, where from time immemorial the highest degrees of civilization and luxury have been attained. In the torrid zone, the disease is unknown, but sporadic cases appear in the borders of the tropics, and they multiply as the centres of population in the most favored northern regions are approached. For purposes of comparison Europe may be divided into three parallel bands extending from east to west. The first comprises the borders of the Mediterranean Sea, including Spain, the south of France, Italy, Sicily, Greece, and Turkey. Throughout this zone the climate is semi-pelagic and tolerably uniform; the people lead an open-air life, and are poor and temperate. Among them gout is practically unknown excepting occasional cases among the luxurious denizens of the great commercial cities and aristocratic capitals, such as Lisbon, Madrid, Marseilles, Genoa, Rome, Athens, and Constantinople. Among the Mohammedan inhabitants of Turkey, Syria, Egypt, and the north of Africa, the disease is unheard of by reason of the poverty and sobriety of the Oriental population, to whom alcoholic stimulants are forbidden by their religious teachers.

Throughout the remaining countries of continental Europe, excluding Holland, gout is not an uncommon malady, though by no means of frequent occurrence. In France it is in the large cities and among the cider-drinking Bretons and Normans of the west that it is best known. It is more frequently found in the north and northeast than in the rougher and poorer regions of the central territory of the republic. In the rich Champagne country in Lorraine and Burgundy, where good living abounds, gout claims frequent victims. In like manner, the disease flourishes in the rich cities of Germany along the Dutch frontier, and upon the Baltic coast, while it is rarely experienced by the impoverished peasants of the interior and in the direction of the Russian border. In the whiskey-drinking regions of the north of Europe, in northern Russia, Lapland, and the north of Sweden and Norway, gout is seldom known; but in the wealthy cities of southern Scandinavia and Denmark, it is not infrequent. So, also, it appears among the comfortable residents upon the "blacklands" of eastern and southern Russia, where a productive soil permits a considerable degree of luxury.

The third section of Europe, comprising the kingdom of Holland and the British Islands, forms the true paradise of gout. Under a gloomy sky, where the cold, damp winds of the ocean are perpetually flooding the atmosphere with foam from the sea, an immensely wealthy population is crowded within a narrow compass. Upon no other equal space of the earth's surface can be found such an accumulation of all the appliances of luxury. Owing to the character of the climate these comforts must, for the greater part, be enjoyed within doors, by the perpetual fireside, remote from the open air. As a consequence the number of gouty patients is much greater than elsewhere. It is impossible to effect a statistical comparison, because the majority of arthritic patients belong to the upper classes, and are not subject to enumeration and classification like the poor who are compelled to seek relief in the public hospitals. But, even when the statistical returns of the hospitals are compared, the great pre-eminence of England in the matter of gout becomes at once apparent. Ebstein, comparing the returns of the Munich hospitals with those of London, found that among 4,670 Bavarian patients there were only 11 who suffered with gout, while among 4,695 Londoners there were 97 who had the disease. In the Parisian hospitals a case of gout is hardly ever seen. It is, however, a noteworthy fact that all parts of the British Isles do not equally share these morbid privileges. Among the whiskey-drinking Scotch and the potato-eating Irish, despite the atrocity of their climate, gout is rare compared with its prevalence among the beer-drinking English.

Upon the continents of North and South America, the distribution of gout follows the same course that has been observed in Europe. Seldom witnessed in the southern States of America or Mexico, its occurrence becomes more frequent as one approaches the valley of the St. Lawrence. But it is rarely encountered among the hardy and temperate farmers of the country; it is among the wealthy and luxurious children of the newly rich who inhabit the great cities of the sea-coast and the humid shores of the great lakes that the disease in its pronounced articular form is beginning to appear. Upon the great plains and among the mountains of the far West it is practically unknown. The same description applies to the states of South America—gout is unknown among the peasantry, and only occasionally manifests itself among the opulent classes in the large cities. In the islands of the West Indies the indolent inhabitants rarely suffer with gout, probably as a consequence of their comparatively temperate habits and life in the open air. Throughout the torrid zone the malady is unknown, for the same reasons. Consequently, the inhabitants of the greater part of Africa, the whole of India, Siam,

Cochin-China, and the larger portion of China, Australia, and Japan, enjoy an almost perfect immunity from the incidence of the disease. Among the islanders of the Indian and Pacific Oceans, although a tendency to obesity is not uncommon, its articular congener is not experienced. It is said that among the numerous English residents of India, but few suffer with gout. This is probably due to the youth and great activity of that population, made up chiefly of laborious officials, soldiers, and adventurers eager for gain. As a contrast may be cited the frequency with which gout occurs among the elderly and opulent English who congregate in Madeira and other sub-tropical health resorts. The same thing may be observed among the wealthy inhabitants of Egypt or South Africa whenever they yield to the seductions of luxury.

Climate.

The influence of climate, though not wholly decisive as to the incidence of gout, is very great as a determining cause. In warm countries copious perspiration serves to evacuate the peccant matters that circulate in the fluids of the body. The heat of the atmosphere retards the oxidation of the tissues, and reduces the desire for food, so that there is less nitrogenous refuse for disposal. If vigorous intruders from the regions of the north attempt to eat and to drink as they have done in their native countries, they soon die of inflammation of the liver and gastro-enteric tract before they have time to attain the articular result toward which their gastronomic efforts are directed. Consequently, the condition upon which acute gout is dependent for its evolution cannot exist, and the disease remains unknown. But the masked forms of latent gout and the allied diseases that are connected with the arthritic diathesis are not uncommon among many of the people in the sub-tropical and temperate regions of the earth. Thus, calculous disorders are comparatively frequent among the inhabitants of Central Asia, from Turkey to China; and among the Americans "lithæmia" is frequently experienced, while rheumatism prevails everywhere, and falls most impartially upon rich and poor.

Judging from statistics—and there we have a brilliant illustration of the errors that grow out of reliance upon the statistical method without check or counterpoise—the Dutch and the English are the human families who exhibit the greatest predisposition to gout. Undoubtedly, they furnish the largest contingent of sufferers; but this is due not so much to their nationality as to their environment and habits of life. The peasants of Scotland and Ireland, living on oatmeal and potatoes washed down with cold water that is only oc-

casionally tempered with whiskey, never contract the disease. It is unknown among the energetic farmers of America. But, if these country people by any accident attain to affluence, if the temperate and laborious inhabitants of Asia and the Orient are placed in circumstances that permit the indulgence of unrestrained appetite and indolence, they quickly accumulate fat, and become gouty like any other votary of leisure and luxury. Even in Africa and Polynesia, where gout is unknown among the common people, obesity and gout are reckoned as enviable insignia of rank.

Mode of Life.

The effects of diet and modes of life are by far more potent than the influences of race and climate in the production of gout and its congeners. It is true that heredity plays a great part in determining the incidence of the disease in certain families. Living for generation after generation under the same faulty conditions of hygiene and dietetics, a morbid predisposition becomes more easily established, so that it really appears to the superficial observer as if the disease itself were handed down from parent to child. But, as will be more clearly evident when we pass to the study of the nature of gout, it is not the disease that is transmitted, it is the environment and the conditions of existence that are perpetuated; and they reproduce the malady in those who are subjected to their influence. For this reason it is possible by a change of habits to eradicate gout from a family or a nation. The history of the Roman Empire is exceedingly instructive in this particular. During the period of unbridled luxury that followed the conquest of the world, the Romans suffered severely with gout; but with the ruin of the empire and the disappearance of wealth before the invading Huns and Goths and Arabs, the disease declined, and is now prevalent in Italy and the Orient only among the few opulent citizens who neglect the laws of health and the precepts of the Koran. With the growth of temperance and the diffusion of hygienic knowledge, gout is in Europe becoming everywhere less common. The great improvement in all the conditions of life that has been effected during the nineteenth century has diminished the amount of suffering from diseases of nutrition, so that everywhere upon the continent there has been less gout than in former days. The wider diffusion of the comforts of life is also attended by less of their abuse on the part of those who formerly monopolized all the good things of the earth. These facts serve to illustrate the superior influence of personal habits over all considerations of race and climate.

Heredity.

Of all the personal influences that favor the incidence of gout, heredity is one of the most important. All the older writers insisted upon this as a most potent factor in the evolution of the disease from generation to generation. It is noticeable, however, that hereditary antecedents are more conspicuous in England and Holland, where gout is frequently encountered, than in France and the south of Europe, where it is comparatively rare. Thus, Gairdner found, among 156 patients, 140 who had descended from gouty families. Bouchard, on the contrary, could discover only 40 per cent. of his cases who were similarly connected. Obviously, this must be true of a disease which is not absolutely transmitted, but is chiefly dependent upon individual behavior. The word heredity must be understood in connection with gout as a convenient designation for certain habits, modes of training, and occupations that tend to become permanent in certain families or lines of descent. In this sense, heredity exercises a powerful influence upon the constitutions of the several members in a given line of descent, so that a tendency to particular maladies becomes ingrained in the structure and functions of the organs that have been thus moulded. In this way is prepared the field for the manifestation not only of gout, but of all other allied diseases of nutrition, such as gravel, biliary lithiasis, asthma, neuralgia, obesity, diabetes, and articular inflammations. Hutchinson, Dyce Duckworth, and others have noted the interesting fact that the age of the father has a decided effect upon the heredity of gout. When the male parent is young and but recently attacked by the disease, the children who are then begotten will often escape the transmitted predisposition, or will manifest its signs in a minor degree. But the later children will exhibit the tendency with a progressively increasing severity. This is exactly the reverse of what is often observed in syphilis, a disease that is usually contracted in early adult life, and manifests its greatest intensity very soon after infection, gradually subsiding and progressing toward latency as life advances. The earlier-born children of a syphilitic parent, consequently, receive the disease in full intensity, while the later offspring either escape altogether, or exhibit only the milder forms of the malady. Syphilis, like all infectious diseases, tends toward recovery as life proceeds; but gout becomes more inveterate and malignant with the lapse of time; and, consequently, the offspring of its victims are successively representative of the downward course of their progenitors. Many examples of this family decadence have been noted from the days of Sydenham to the present time.

Acute gout, followed by uratic deposits in the joints, appears to be more frequently transmitted by the father than by the mother. According to the often-quoted statistics gathered by Scudamore, among 263 cases of hereditary gout 181 were derived from the father, and 58 from the mother, while only 24 were children of parents who were both gouty. But this disproportion seems less remarkable when we take note of the greater frequency of articular gout among men, and the fact that when it does attack the members of the female sex it usually makes its appearance after the close of the child-bearing period. If, however, we look beyond the sphere of articular manifestations, we shall find that anæmia, neuralgia, lithiasis, asthma, bronchitis, and the allied diseases that depend upon the arthritic diathesis are perhaps quite as common among women as among men. In gouty families, the males develop articular disorders in addition to the minor forms of arthritism, while the females less frequently reach the most conspicuous manifestations of the diathesis which they also have inherited. It is still an open question whether the transmission of the gouty predisposition is more likely to occur when both of the parents are affected with the disease at the time of maternal conception. Such a result seems highly probable, but its proof is very difficult. The explosion of gout is liable to so many caprices that are dependent upon accidental and variable causes that it is extremely difficult to trace their operation. That the children of a gouty couple should be exposed to greater errors of diet and hygiene through the traditional habits of their ancestors in accordance with which they are educated seems very likely. But, so changeable are the conditions of life in many families, that hereditary influences may be wholly or in part counteracted by the mutations of fortune and the consequent abandonment of faulty habits, or they may be intensified by the attainment of new opportunities for intemperance and self-indulgence.

For similar reasons it is impossible to decide whether gout becomes modified through the course of successive generations. Misled by a fancied analogy derived from observation of the infectious diseases, some have imagined that gout can become attenuated and die out in the course of descent through time. This, however, is only possible in diseases that depend upon the transmission of an infective agent. The infective germs are gradually attenuated through contact with healthy tissues, and tend to become innocuous. Were it not for fresh infection from sources external to the body, it is probable that all bacterial diseases would in time thus become extinct. But gout is not thus derived by the transmission of a contagium. Only the enfeebled and susceptible constitution is inherited.

The subsequent manifestations depend chiefly upon individual and personal causes that may or may not be called into action. For these reasons the course of gout through a series of generations will exhibit great variations. Sometimes the disease seems to become masked and to assume visceral forms for successive periods of family life. In other instances, it disappears for a generation, and then reappears with all its pristine severity in the next. Rarely, however, does it become latent without the manifestation of one or more of its congeners, eczema, neuralgia, bronchitis, asthma, lithiasis, etc., among those who have escaped its full force.

Age.

Gout is almost always a disease of adult age. But it has been occasionally experienced by children. Boerhaave observed such cases, and others have been reported by Schenck, Debout, and Rendu, occurring in children between the ages of seven and seventeen years. In the majority of cases, however, it is in the fourth decade of life that the first attack is experienced. In this particular the following statistics, borrowed from Scudamore, are very instructive:

First Attack of Gout.

8 years	1	30 to 35 years	105
12 "	1	35 " 40 "	89
15 "	1	40 " 45 "	64
16 "	1	45 " 50 "	54
17 "	1	50 " 55 "	26
18 "	5	55 " 60 "	12
19 "	3	60 " 65 "	8
20 to 25 years	57	66 years	2
25 " 30 "	85	Total	515

From this table it appears that considerably more than half the cases were first attacked between the ages of twenty-five and thirty-five years; while the largest number in any period of five years occurred during the first half of the fourth decade of life. Pâtissier has reached the same statistical result, and has also noted the interesting fact that among the victims of hereditary gout the first attack is most frequently experienced at the age of thirty-four, while in cases of the acquired disease the favorite age is thirty-eight, showing that it takes four years longer to subdue a virgin soil than to overcome a constitution that has been enfeebled in advance by ancestral excesses.

Among the very aged articular gout is almost as infrequent as among small children. Yet Sir A. Garrod has seen the disease in a

number of instances after seventy, and Blackmore relates the history of a patient who at seventy-eight suffered for the first time with gout. In the majority of such cases, there are special reasons that determine the tardy onset of the malady. They are usually cases in which the effects of luxury have been held in check by the exercises of an active life in the open air, until at last, during the concluding years of a long existence, the individual retires from business, but continues to indulge without stint in the pleasures of the table. Under such circumstances disorder soon arises; and, if articular manifestations be not developed, the minor evidences of uric-acid accumulations are sure to appear with all that tendency to subacute intensity and sluggish progress which is characteristic of gout in old people.

Sex.

Women are far less liable than men to the incidence of gout. Even among the English, Scudamore could find but 12 females out of 68 cases of the disease. Durand-Fardel and Pâtissier, in a total of 580 cases, numbered only 20 women. If, however, the allied diseases, lithiasis and arthritis deformans, were taken into account, the disproportion would not be so glaring, for these are the forms of arthritism that are most frequently experienced by the female sex. A certain connection between the cessation of the menses and the manifestation of gout in the female has been asserted from time immemorial. It is probable that menstrual suppression does operate somewhat unfavorably in this respect. In the majority of cases that are uncomplicated by local disease of the female organs of generation the occurrence of pelvic disturbance is due to gout in its masked varieties. In many instances the cessation of the menstrual flux seems to close up an outlet for "peccant humors," and gout attacks the joints. It is a notable fact that the age of puberty is for the female another epoch at which arthritic manifestations are not uncommon. The frequent occurrence of gouty headaches at the time of the monthly periods indicates that menstruation must not be considered a shield against gout. In fact, among young women who are predisposed to arthritic disease the occurrence of articular crises seems to be quite independent of menstrual disorder, so that it is very likely that the frequent development of gout that is witnessed after the close of sexual life in the female is fully as much the result of advancing years as of the cessation of the menses.

Gout does not seem to be favored by any particular type of constitution. It attacks the corpulent and the lean-favored, the sanguine and the bilious. But it is noteworthy that in the majority of cases its

victims give evidence of good living, either through a tendency to obesity or through the dyspepsia that results from over-feeding and an inactive life. Scudamore, who is nothing if not statistical, found, among 156 patients, 126 who were more ponderous than the average individual. The type of the gouty manifestation conforms very closely to the general constitution of the patient. Vigorous, florid, and sanguine subjects have acute inflammatory attacks of the disease; bilious and dyspeptic people suffer with hemorrhoidal and hepatic crises; while those who possess a weakly and nervous organization exhibit all the phenomena of nervous gout: neuralgia, abdominal pain, muscular cramp, asthma, angina pectoris, headache, etc.

Diet.

Although it is evident that many causes contribute to the development of gout, there is none that compares in efficiency with excess in eating and drinking. We have seen that the disease is most prevalent in countries where wealth and luxury abound. It is also apparent that in those lands where it is common, the incidence of gout is most frequent among the luxurious classes of society—especially among the newly rich, who have recently acquired unlimited means of gratifying their appetites and passions, without having at the same time learned discretion in the enjoyment of good fortune. These people, who have usually risen rapidly from the lower ranks of society by reason of remarkable physical energy, carry into advanced life and leisure the excellent appetites that were the delight of their youth. Continuing thus to gorge themselves with belated delicacies long after the close of active existence, they fall victims to arthritic disorder, and the children of their old age yield themselves an easy prey to the influences in the midst of which they were begotten. For these reasons gout is more often witnessed among the successful middle-class citizens than in the families of an ancient nobility to whom the long experience of wholesome living has become an ancestral heritage. But in any situation, it is impossible to lead a life of indolence and gluttony without being sooner or later called upon to pay the penalty. It was not without a reason in the nature of things that men like the great Napoleon have found themselves continually impelled to break away from consuming intellectual labors, to seek in hard riding over the country a means of relief from the rising tide of arthritism that threatened to overwhelm their tissues. The physiological chemists have shown that every excess in the use of flesh food causes a corresponding increase in the production of urea and uric acid. If the amount of muscular exercise be reduced

to a minimum, the rate of oxidation falls, and the nitrogenous refuse —uric acid—remains in a condition that hinders its elimination through the kidneys. The urates and their congeners accumulate in the system, and finally produce a critical explosion by which they may be for a time wholly or in part ejected from the body. But when exercise stimulates the circulation, causing the transportation of an increased amount of oxygen to the molecular basis of the tissues, the oxidation of uric acid into soluble forms of nitrogenous refuse proceeds with greater completeness, and the system is cleared of urates, to the great relief of the individual. Hence the instinctive longing for action and muscular effort that characterizes the consumer of animal food during the early portion of his career. Hence the fondness for athletic sports, hunting, and fighting, that characterizes the well-fed eater of flesh. So long as he can keep the field and follow the hounds, all goes well; but when youth has departed, and he can only follow his army in a coach, the end is near, and he must smother in his own excretions.

Besides the accumulation of urates under such circumstances, another most injurious complication arises—the overloaded stomach fails to accomplish its functions, and the nitrogenous elements of the food are but imperfectly digested. Hence a surcharge of undigested substances along the whole course of the alimentary canal, followed by the formation of various toxalbumins and ptomaïnes that are absorbed into the circulation and exert a poisonous influence upon the functions of every organ in the body. From this cause results a further hindrance of the process of oxidation, so that the nitrogenous elements of the tissues are not fully transformed into urea, but tend to accumulate in the form of imperfectly oxidized products, of which uric acid is the most conspicuous example.

The character of the food that is habitually consumed largely determines the amount of urea and uric acid that is produced in the body. These nitrogenized bodies are derived most abundantly from the nitrogenous aliments; consequently, the consumption of animal food exercises a direct influence upon their formation. Other things being equal, the more meat one eats the more likely is he to become gouty. In this fact lies one of the causes of the prevalence of gout among the English. From the dawn of history they have been noted for the quantity of flesh that is consumed in their dietary. The beef-eaters of Old England were no figment of poetic fancy—they were, and still are, a most solid and substantial reality. In the lists of viands provided for the daily meals and banquets in the good old times, bread and fruits and vegetables hold a very insignificant place alongside the mighty roasts and joints and chines and jowls and ven-

ison pies that chiefly occupied the attention of the rubicund trencher-men. A surcharge of uric acid was the inevitable result of such a mode of living. It is true that the excessive use of sweets and starches may lead to a somewhat similar end, but in a rather indirect way. Obesity is the primary consequence of a highly carbonaceous diet; but the alimentary tract is in many instances better adapted for the digestion of meat than for the disposition of sugars and starches. These also require for their oxidation so large a proportion of the oxygen that enters the tissues that there may be an insufficient residuum available for the complete oxidation of uric acid into urea; and thus a vegetable diet may actually lead indirectly to an accumulation of urates in the body. The same thing is theoretically true of the fats as an article of diet; yet the blubber-eating Esquimaux never have gout. This is owing to their active exercise in the open air, and to the frigidity of their climate. A low temperature of the air expedites all the processes of oxidation in the tissues, in order to maintain the normal heat of the body; and thus the excessive formation and accumulation of uric acid and fat are prevented.

Fresh fruits and vegetables are generally to be recommended for the nourishment of the gouty. But such as contain oxalic acid and its compounds (rhubarb, pie-plant, beets, spinach, sorrel, etc.) should be avoided because of the tendency of the acid to attack the tribasic phosphates in the tissues, reducing them to the condition of soluble acid phosphates which quickly appear with oxalate of calcium in the urine, to the decided detriment of the patient. This, it should be remembered, is not the only source of oxalic acid in the body. Whenever the oxidation of uric acid is retarded oxalic acid appears; consequently, the presence of oxalates in the urine is indicative of imperfect combustion of nitrogenous compounds in the tissues, unless it can be shown that their presence is only the accidental result of a diet that is surcharged with those salts.

From these observations, then, it appears that a nitrogenous diet is the form of aliment that chiefly predisposes to the occurrence of gout; but that the excessive consumption of starches, sugars, and fats —the alimentary carbohydrates and hydrocarbons in general—may indirectly effect the same result by impeding the oxidation of nitrogenous compounds. This, however, is not likely to occur, excepting in the case of individuals who consume large quantities of nutritious food and do not by active exercise promote the full exchange of oxygen in their tissues.

In his valuable work on "Uric Acid in the Causation of Disease" (second edition, 1894) Haig has shown that uric acid as excreted normally in the urine is derived from the oxidation of nitrogenous sub-

stances that have been received into the body, and also from the urates that are always present in the meats, soups, gravies, etc., that are ingested with the food. It thus becomes possible to vary the quantity of urates that are excreted in the urine, and to study at pleasure the effect of artificially loading the blood with uric acid, or the reverse. When the blood is thus overcharged, the quantity that passes into the urine, if due alkalescence of the circulating fluid be maintained, is sufficient to clear the system in a short time; but, if the blood be in any way rendered more than normally acid, the surplus urates are retained in the tissues, are not conveyed to the kidneys, and do not appear in the urine. When this occurs in a susceptible individual, pricking pains may be felt in the joints, an attack of headache may be experienced, and other of the premonitory symptoms of gout may be developed. Thus it can be shown that many of the phenomena that are associated with gout can be produced by the ingestion of uric acid and the nitrogenous compounds out of which it is formed in the body.

From the remotest antiquity the deleterious influence of wine and other fermented beverages upon the production of gout has been a matter of constant remark. Sir A. Garrod inclined to the belief that acute gout could not exist in their absence. It is not, however, by virtue of the alcohol which they contain that these liquids exercise their baneful influence. The inhabitants of southern Europe, who drink large quantities of wine, seldom suffer with gout. The same thing is true of the consumers of brandy and whiskey in northern Europe and Scotland. They are victims of alcoholism to a frightful degree, but of gout—hardly ever. In fact, the chronic gastritis that has its origin in the use of distilled liquors destroys the appetite, and effectually prevents that inordinate consumption of food which is one of the prime requisites for the evolution of gout.

Among the wines that are used upon the tables of the rich, the researches of Garrod have also indicated a difference. The rare old crusted ports and sherries lead the way as the most efficient adjuvants in the production of gout. Then, at a considerable distance, may be placed the lighter wines of Burgundy and Champagne; last of all those of the valley of the Rhine and its affluents. Still, it is an interesting fact that in the wine-growing countries the laborers who indulge to excess in their use do not become gouty—they sink into a condition of chronic alcoholism. Only those who at the same time over-eat and over-drink themselves fall victims to the arthritic disease. Sweet and effervescent wines do indeed aid in its development, but they cannot create the malady without the concurrence of an immoderate consumption of flesh and the other dainties of the

table. It must never be forgotten that gout is not the consequence of alcoholism but of gluttony. For this reason the use of malt liquors is especially injurious. Porter, ale, and beer contain a considerable quantity of sugar, dextrin, etc., besides the alcohol that is present. The lower price at which these beverages are furnished leads to their inordinate consumption—sometimes to the extent of forty to sixty glasses a day. Budd stated that among the watermen of the Thames it was a common thing to drink twelve quarts of porter every day. Naturally they rapidly became gouty, though not handicapped by hereditary predisposition, since the majority of them were Irish, who were brought up in abstemious poverty. Scudamore, Watson, Todd, and other English authors have noted the strong predisposition to gout that prevails among the people who contract a fondness for porter. Similar results have been remarked in Holland, Belgium, and other beer-drinking countries. There is, however, a very important difference in the effects that are produced by the various kinds of malt liquor. Porter, a compound of hops and torrefied malt, has by far the worst reputation. Ale, a beverage obtained from non-carbonized malt, though often containing a larger percentage of alcohol than exists in porter, is less deleterious. In Germany, notwithstanding the enormous consumption of lager-beer, gout is an infrequent disease. If valued according to their nutrient qualities, porter obtains the highest rank, though containing less sugar and alcohol than ale. The German beers contain the least of all. In England and Holland, moreover, the people are more abundantly nourished than in Germany and in many parts of France, consequently their nutritious beverages promote over-feeding and its consequences. The hot summers of the Continent must be also taken into consideration, for the copious perspiration that they induce serves to relieve the overburdened kidneys, while the inhabitants of the damp and chilly lowlands of Holland and England obtain comparatively little help from that source. For this same reason, probably, the inhabitants of the western coasts of France suffer more severely with gout than the dwellers in the southern and central portions of the republic. Some have thought that the difference should be ascribed to the extensive use of cider among the Bretons and Normans; but in other countries where cider is largely consumed, as was formerly the case in the New England States of America, gout is seldom known. Its excessive use produces alcoholism, just as vinous excess among the laboring classes in wine-raising countries is followed by that result. Something more than the mere drinking of alcoholic beverages is needed for the development of gout. There must be taken with the drink an abundance of nitrogenous food before the symptoms of arthritism can be induced. These con-

ditions are seldom realized among the laborious peasantry; consequently, it is among the rich and idle classes, even in cider-drinking countries, that we find the manifestations of a gouty predisposition. While it is true that alcoholic beverages facilitate the development of gout, and that the fermented malt-liquors are more prejudicial than distilled mixtures of equivalent alcoholic strength, it is incorrect to suppose that they can alone produce arthritic disease. Alcohol certainly retards the processes of oxidation in the tissues, but unless their protoplasm is, by reason of excessive nitrogenous feeding, surcharged with substances that must be thoroughly oxidized before they can be normally eliminated, there can be no accumulation of uric acid—hence no gout. It has long been known that the use of brandy and other distilled liquors causes a decided reduction in the quantity of urea that appears in the urine. Haig has shown that the relation between the formation of urea and of uric acid is comparatively uniform—hence there will be less uric acid under such circumstances. A part of this reduction is probably due to the catarrhal state of the alimentary mucous membrane, and the consequent loss of appetite; but it cannot be thus entirely explained. The parallel reduction of urea and of urates in the urine indicates a condition in which a tendency to uricæmia does not exist. The mere use of alcohol as a beverage, therefore, cannot be counted among the causes of gout. But when alcohol is drunk in a watery solution that is also charged with nutritious substances, such as are found in malt liquors, a step has been taken in the direction of a nitrogenous surplus in the tissues. And when to all these substances an abundant flesh diet is added, a very large amount of urea and of uric acid must be eliminated in order to prevent a storage of urates in the body, and the final explosion of arthritic disease as the consequence of their deposit in the joints. It is this retarded elimination that is effected by damp weather, a chilly atmosphere, immoderate eating, alcoholic beverages, and lack of exercise.

Bodily and Mental Exercise.

The neglect of muscular exercise is, indeed, one of the most potent causes of gout. Even in cases that do not reach the final stage of articular crises, the lack of exercise often leads to the development of the allied disorders and premonitory symptoms of the disease. Obesity and lithiasis are of frequent occurrence among women and among men who indulge their appetites while leading a sedentary life. Such people suffer with dyspepsia, constipation, hemorrhoids, asthma, bronchitis, headache, neuralgia, flushing of the face, loss of

memory, incapacity to fix the attention, universal debility of mind and body. Somnolence after meals and insomnia at night are among the common experiences of such patients. So long as youthful vigor remains, these conditions may be temporarily dispelled by a resort to active exercise and elimination. A season at Saratoga or Carlsbad, a course of mountain climbing, or a fishing excursion along the sea-coast will for a time postpone the evil day; but, if the injudicious system of alimentation be not radically reformed, the advance of years will destroy the inclination to activity, and a weakened heart or a contracting kidney will finally render all forms of prolonged muscular exercise impossible, through the establishment of the arthritic diathesis, if not through the actual manifestation of articular gout. This is the condition into which so many fine ladies and men of high standing in the professional and commercial classes have insensibly descended, without knowledge of the true character of their malady. Under the influence of sedentary habits and advancing years, fatigue of every variety becomes an exciting cause of gout. Long walks and unusual muscular exertion are frequently followed, in predisposed persons, by an outbreak of articular inflammation. It is probable that under such circumstances the joint or joints become overcharged with the acid products of active exercise, so that the circulating fluids in the affected tissues cannot hold the urates in solution, and they are at once precipitated upon the spot, and there serve to excite inflammation. But similar consequences may follow upon the occurrence of fatigue of a more general character. Venereal excesses have always been accused of producing gloomy results in gouty subjects. Even among comparatively young people, if they have acquired the arthritic predisposition, a course of debauchery is very liable to induce the disease. This may be in part the result of the intemperance in eating and drinking that so frequently accompanies this form of dissipation; but a certain appreciable influence is unquestionably due to the exhaustion that follows the act of copulation under such conditions. Among elderly people there can be no doubt regarding the disastrous effects of such exercises. After middle life, as the individual enters the sixth decade of years, he must practise temperance in all things if he would not find himself gradually sinking into gout or its minor manifestations or allied maladies.

In like manner, great intellectual exercises; grief, anger, disappointment, or any form of psychical disturbance, may operate to favor the development of gout. As in the analogous over-exertion of the nervous system that accompanies the venereal act, these violent explosions of cerebral and spinal protoplasm serve to depress the functions of assimilation and nutrition, to retard the process of oxi-

dation in the tissues, and to hinder the evacuation of uric acid through the kidneys. The system may thus become overcharged with urates, and the various phenomena of gout are developed. The allied diseases, lithiasis and diabetes, are not infrequently fostered by the same cause; hence the common occurrence of these nutritional disorders among men who are active in political and commercial life. Strong in body, energetic, and successful in the accumulation of money, they indulge their appetites, and with advancing years do not learn to restrain their desires. Finally, reverses meet them, and anxieties without number leave them no opportunity for rest. Under the influence of these excitements, all the functions of nutrition, from mastication to evacuation of the bladder and rectum, fall into disorder. The inevitable consequences are indigestion, gastro-intestinal fermentation, acid dyscrasia, retarded oxidation, phosphaturia, oxaluria, mellituria, lithiasis, nephritis, asthma, bronchitis, neuralgia, neurasthenia, melancholia, gout—one or more or all developed, in succession or together, in the person of the prematurely old man. Thus it is that so many brilliant and successful men have been driven from public life, and have been compelled to pass what should have been their best days in obscurity and inaction.

Season.

The change of the seasons produces a decided effect upon the manifestations of gout. The disease is most frequently experienced in the spring and autumn of the year. Various causes unite to bring about this result, and it cannot be ascribed to any single fact. It is during the vernal and autumnal months that sudden changes of atmospheric temperature are liable to interfere with the normal discharge of heat from the body by sudden excitation and as sudden arrest of the cutaneous perspiration. With every change of wind from north to south, and *vice versa*, in many countries the individual finds himself either reeking with sweat, or compelled to return to winter clothing in order to protect the body from the dry cold air. When the dry and constant heat of the summer has become established, the heat of the body is regularly discharged through the perfect evaporation of the perspiration as rapidly as it is formed. Hence the greater comfort that is experienced in a hot and dry atmosphere than in a humid though relatively cooler air. In like manner, the steady abstraction of heat that takes place in the cold, clear days of midwinter causes a feeling of vigor and well-being that is not experienced during the warm and chilly seasons before and after the frosty months of the year. The reason of this is to be found in the fact that the oxidation of

tissue-protoplasm is promoted by the normal discharge of heat from the body. Within normal bounds increased metabolism causes an increase of energy in the body and removes obstacles to the liberation of force. Uric acid and other forms of refuse are rendered more soluble by transformation into water, carbon dioxide, and urea, so that there is less accumulation of protoplasmic débris in the body. Under such circumstances, the detention of urates is less likely to occur, and the manifestations of gout do not appear. Some account must be taken, also, of the increased rate of the circulation during the dry heat of summer and the dry cold of midwinter; the heart beats with greater force, and the blood penetrates the tissues with greater effect. The result of increased atmospheric pressure during periods marked by a high barometer is of the same character. With increase of pressure the amount of oxygen that is inspired is increased and metabolism is promoted. But during the changeable weather of spring and autumn there is no constancy in these conditions, and the nervous system that has been rendered over-sensitive by the establishment of the arthritic diathesis reacts violently and tumultuously under unfavorable circumstances for the preservation of health, and disease is manifested. This result is especially liable to occur after a winter of dissipation, or of tiresome intellectual labor by which the system is overloaded with the products of fatigue. Still more unfavorable are the conditions when, in addition to all these causes, luxurious living has damaged the digestive organs with alcohol and an excess of nitrogenous food. It must not be forgotten that every hearty meal, in which meats, soups, and gravies are conspicuous, serves to introduce into the blood a notable quantity of ready-made uric acid which may suffice, with what has been already stored in the tissues, to excite an explosion of gout. Hence the frequency with which, in the spring of the year, a grand dinner or a wine supper is followed by an articular crisis in the person of a subject who is predisposed to the disease. Haig tells us that he can thus excite articular pains in his own limbs at any time. Sir A. Garrod has repeatedly witnessed similar phenomena after a few glasses of champagne or port. Some patients cannot eat a bunch of grapes or a plate of gooseberries without similar consequences. Garrod, indeed, considers the occurrence of articular inflammation after indulgence in fermented drinks as pathognomonic of gout. Thus it is rendered evident that gout is a continual malady, in which the articular crises are only the most conspicuous manifestations of the condition of disease which, for the sake of convenience, is called the arthritic or gouty diathesis. Once acquired, the predisposition remains permanent; and, when completely established, the patient becomes so unstable that slight deviations from the ordinary

routine of life and health are sufficient to precipitate an acute attack. In the female sex the occurrence of pregnancy, like venereal indulgence on the part of the male, is sometimes sufficient to bring on an attack. Slight ailments, as a sore throat or a coryza, may be followed by articular inflammation; though it is very probable that these may be simple prodromes of the attack, just as they frequently are related to the kindred malady, rheumatism. Strong emotions of a depressing character and unusual intellectual efforts often act in a similar way as excitants of the disease. The great Sydenham has recorded the fact that whenever he applied himself with more than ordinary vigor to the work of writing and study, he provoked an attack of the disease with which he was personally so familiar. Of other scholars not a few can report a similar experience. Fatigue of every kind must, therefore, be reckoned among the occasional exciting causes of gout.

Poisons.

The interesting observations of Haig have made more prominent than formerly certain facts regarding the influence of a considerable number of chemical agents in the production of arthritic symptoms through their hindrance of the excretion of uric acid. Chief among these substances are "acids, iron, lead, lithia, manganese, calcium chloride, acid phosphate of sodium, some sulphates, chlorides, etc., and many substances which directly or indirectly raise the acidity or otherwise form insoluble compounds with uric acid, as opium, cocaine, mercury, the iodides, antipyrin, ammonium, the nitrites, some hyposulphites, strychnine, and many other less well-known substances" ("Uric Acid in Causation of Disease," second edition, pp. 23, 24). These agents have the common property of repelling uric acid from its solution in the blood, and driving it into the tissues where it is retained and is held in a state of inertia. In this way they give temporary relief from the symptoms that are excited by the circulation of urates dissolved in the blood. But this relief is only provisional; after a time the accumulation about the joints becomes sufficient to excite local disorder; or an increase of the alkalinity of the blood causes it to take up an excess of urates which produce general pain and distress as they are transported through the body on their way to the kidneys. Probably the uric-acid compounds are not the only offending substances, but also other nitrogenous compounds and the products of faulty metabolism in the liver must be taken into account. Uric acid may be conveniently employed as a general term including all the forms of peccant matter that originate in the body, and contribute to the development of gout.

Conspicuous among the chemical agents above mentioned is lead. Sir A. Garrod noted the fact that rather more than one-quarter of his gouty patients in the hospital had suffered with symptoms of lead-poisoning, usually contracted in the course of their work as house painters. The precision with which this distinguished author determined the relationship existing between the two diseases gave occasion for extensive investigation of the subject. It was then discovered that older observers had recorded the same fact—notably Barlow (1822), Parry (1825), and Todd (1843). But these observations had produced no abiding impression; and the whole matter remained in the shade until the appearance of Garrod's paper in the Medico-Chirurgical Transactions, Vol. XXXVI., 1854. Since then the relation of lead-poisoning to gout has been carefully studied by numerous observers. Opinions, however, have been for a long time divided, since it is not everywhere that conditions exist for the coincident development of the two diseases. In Scotland and Germany gout and lead-poisoning are too infrequent to admit of an extended comparison. In France, where lead-poisoning is sufficiently common, gout is a rare disease. It was in England, before the introduction of the great hygienic improvements that have done so much for the health of the population, that the whole subject could be most profitably studied. The question that was presented for solution raised the inquiry as to the possibility of producing gout by the direct toxic influence of lead. This has been denied by the majority of observers, while a considerable number have confessed their inability to render a decision. A few have thought that it was possible in certain cases to recognize a directly causative influence in the action of lead. It must be admitted that coincidence of lead-poisoning and gout will satisfactorily account for a portion of the cases. When an hereditary predisposition exists, the occurrence of saturnism may indirectly excite gouty phenomena, just as any intercurrent disease may suffice to arouse the latent diathetic tendencies. The habits of the victims of lead-poisoning are often of a nature that is calculated to create the arthritic diathesis, if it be not already inherited. Thus lead-poisoning has been noted among beer drinkers whose mugs are filled from a leaden pipe and faucet. This has been especially true of those ardent devotees whose thirst has urged them in the morning to imbibe the first tap of ale or beer which had lain all night in contact with the leaden pipe through which it was drawn. Such individuals may easily become both plumbic and gouty. Still, it must be admitted that occasionally the well-marked symptoms of gout are manifested by patients who have led an active and temperate life, who have inherited no predisposition to arthritic diseases, but are sufferers from poisoning with lead. Sir

A. Garrod has shown that the urine of the victims of plumbism closely resembles that which is voided by the gouty. In both cases the urine is scanty, and the quantity of urea and of uric acid is below the normal standard, while the blood and the tissues contain these nitrogenous substances in considerable amount. This, however, is true in certain stages only of the disease. At other periods the quantity of urea and of urates is normal, or in excess of the usual amount. These fluctuations have been noted both in gout and in plumbism. In certain cases, also, chemical analysis of the blood fails to detect the presence of uric acid in that fluid. Here, again, gout and plumbism are alike. The variations in the composition of the urine and of the circulating fluids of the body are exceedingly numerous, and they succeed each other with a rapidity that is surprising to every one who is not familiar with the results of analysis. These facts seem to indicate great similarity between the action of lead and the cause of gout.

When examination of the viscera is made after the death of the patient, the parallel between the effects of gout and of lead is still remarkable. Both produce identical changes in the kidneys and arteries. It is impossible to distinguish between the contracted kidneys of gout and those of lead-poisoning. In both are apparent the same chronic inflammation of the interstitial connective tissue, and the same progressive atrophy of the parenchyma of the organ. Hence the remarkable similarity in the composition of the urine in both classes. In a memoir on this subject Lancereaux (*Archives Générales de Médecine*, Dec., 1881) states that in twenty-four fatal cases of plumbism gouty arthritis was recognized in seven, five of which were verified at the autopsy. In these cases the relationship between the arthritic infiltrations and lead-poisoning seemed quite conclusive.

But Garrod and, more recently, Haig have subjected the question to the test of actual experiment. Giving pills of lead acetate to their patients, they witnessed a diminution of the urinary urates below the quantity that was habitually discharged before the experiment. This result corresponded exactly with their observations in cases of ordinary gout—retention of uric acid leading to the production of uricacid-æmia and the symptoms of arthritic dyscrasia. In the vast majority of cases lead-poisoning is not followed by the articular symptoms of gout; but sometimes it does seem to produce a sufficient predisposition, so that slight occasional or accidental causes are found adequate to excite an acute attack, just as such causes operate in ordinary examples of the arthritic diathesis. It is through the agency of lead in modifying the production of nitrogenous waste, and retarding its excretion, that in certain sensitive subjects the establishment of what is equivalent to the diathesis is effected. In this sense lead

may be said to originate gout. The general course of the disease when thus excited is identical with that of the typical articular inflammation. It follows the same law of seasonal periodicity; it affects the great toe by preference, whence it extends slowly to the other joints; and it finally degenerates into the chronic, subacute form that is characteristic of gout in old age. Certain points of difference, however, between saturnine gout and the ordinary variety may be noted. It never breaks out in an individual who is in the enjoyment of good health; it attacks those who have been previously suffering with lead-poisoning, usually in the form of colic, anæmia, and lead palsy. Its onset is rarely ushered in by any other premonitory symptoms, but when once established it occupies a number of joints, very much like rheumatic polyarthritis. The urine, also, which in ordinary gout seldom contains albumin, almost always contains at least a trace in the saturnine variety of the disease. This profound disorder of the kidneys is one of the most characteristic facts in these cases. Instead of continuing for many years to enjoy reasonably good health during the intervals between the attacks, the patient soon degenerates into a condition of chronic cachexia, with articular lesions and renal disorders that only appear at a very late period in ordinary gout. Death usually results from uræmic accidents, such as suppression of the urine, dropsy, convulsions, and coma.

Diagnosis.

Typical cases of acute articular gout are easily recognized. It is only necessary to review the symptomatology of the disease in order to form a picture that cannot be mistaken for anything else. Chronic cases in which the joints of the fingers and toes—perhaps other larger joints also—have become deformed by repeated attacks of inflammation, and by the deposit of urates in the articular structures, are seldom difficult of recognition. But great difficulties may arise in connection with certain unusual or obscure manifestations of the disease. Sometimes many joints are simultaneously attacked, so that the patient appears to be suffering with acute inflammatory rheumatism. Even the most experienced clinical observers have been thus occasionally led astray. Sometimes, again, it is the chronic form of the disease that assumes the garb of chronic rheumatism, progressing by successive subacute exacerbations that involve the joints of the fingers and toes, producing nodosities and deformities that appear to be common to both diseases. Occasionally the autopsy alone, by revealing the presence of urates in the joints, can give precision to the diagnosis. In many instances arthritis defor-

mans has been mistaken, sometimes for rheumatism, sometimes for gout; but this uncertainty can be usually traced to the once prevalent notion that this species of arthritis is an hybrid disease, sharing in the characteristic phenomena of chronic gout and chronic rheumatism.

Very few clinical observers at the present time will undertake to maintain the identity of gout and rheumatism, even in their more obscure and chronic forms. If we pass in review the etiology of the two diseases, we find that while certain events, such as exposure to cold and damp, contusions, sprains, injuries, psychical exhaustion and physical fatigue, may act alike as occasional or exciting causes for either affection, the remote, predisposing, and essential causes are widely different. Gout, even in England and Holland, is a rare disease, while rheumatism is one of the most common. Gout, thanks to an improved acquaintance with the laws of health, is becoming less frequent, but rheumatism is more and more widely diffused. The one disorder is unknown in tropical countries, and is most prevalent where wealth and luxury are enjoyed under inclement skies in a damp and chilly climate; the other is confined to no country or clime, it prevails alike among rich and poor, temperate and gluttonous, indolent and laborious. Exposure to cold and hard work in the open air are safeguards against gout, but they are common exciting causes of rheumatism. The first is a disease that mostly affects the male sex, after the attainment of adult life; but the second strikes both sexes alike, and is even more commonly experienced, at least in its acute and abarticular forms, among children and youth. The personal habits of the individual exert comparatively little influence upon the evolution of rheumatism, while gout is largely dependent upon excessive eating and drinking, lack of exercise, and the intemperate use of fermented beverages.

The morbid anatomy of the two diseases presents equally conspicuous differences. Both are nothing if not articular in their manifestations, but the effect upon the joints differs widely in either malady. In rheumatism the symptoms of local inflammation are most painfully evident, but they rapidly vanish with the subsidence of disorder in the affected joints. The articulations may be repeatedly inflamed without leaving any appreciable trace that can be recognized during the intervals of perfect health that succeed each attack. But in gout, every attack leaves behind it a permanent alteration of structure in the joint that has been the seat of disease. Consequently, the gouty subject after his first crisis can never be considered as perfectly well. He is henceforth more or less of an invalid; and each recurring attack adds to the disorganization of the affected articulations. In chronic gout the joints are enlarged and stiffened by an infiltration

of urates into the cartilages and fibrous tissues that enter into the structure of the joint. In chronic rheumatism it is the extremities of the bones that are the seat of disease—a tedious swelling, inflammation, and deformity of the osseous substance beneath and behind the articular cartilage, while the synovial cavities exhibit no trace of disease greater than is implied by a slight excess of the synovial fluid. Examination of the internal viscera of the body reveals an opposition of signs that is equally convincing. Rheumatism by preference causes pathological changes in the heart and vascular canals; the blood is rich in fibrin, and its corpuscles undergo rapid destruction. But in gout it is uric acid that is present in excess, and the kidneys are the usual starting-point of internal disease.

The clinical features of the two diseases usually exhibit considerable diversity. Rheumatism seizes upon the larger joints of the extremities, either simultaneously or in quick succession. Gout usually begins in the joints of the great toe, and seldom quits the smaller articulations of the foot and hand. Rheumatism is less painful than gout; it is accompanied by less superficial inflammation and desquamation of the cuticle; though it may sometimes produce an equal amount of œdematous swelling about the affected part, it is never attended by the turgescence of the cutaneous veins that is so marked a feature during the gouty crisis. The symptoms that follow invasion of the intracranial organ differ in the case of the two diseases. Headache is less severe and less characterized by lancinating pain in rheumatism than in gout. Aphasia and vertigo are rare events in the former disease, while they are not infrequent in the latter. In rheumatism, delirium, convulsions, and hyperthermia are commonly observed, though seldom witnessed in gout.

These characteristic and almost pathognomonic symptoms that so clearly distinguish the typical cases from each other are less sharply defined and convincing when we are called upon to deal with chronic, subacute, and masked forms of the two diseases. The slowly progressive articular malady which has been described under the names of rheumatic gout, rheumatoid arthritis, or arthritis deformans, has many points of resemblance with senile gout. It was long an open question whether it is an independent pathological entity, or whether it is merely one of the varieties of chronic rheumatism or chronic gout. It is now considered as a separate disease, in which the mimicry of gout and rheumatism is more apparent than real; and in order to avoid confusion with the other species of diathetic arthritis, it seems expedient to omit from its nomenclature all reference to them, giving it the independent title of arthritis deformans. This form of arthritis is frequently hereditary—in this respect resembling

gout. It usually occurs among elderly females, but without any previous influence of intemperance, indolence, or luxury. It is usually, on the contrary, associated with low living, austerity of manners, and laborious occupations, manifesting itself during the decline of life, and slowly progressing without any very evident exciting cause. The articular deformity presents an appearance that is like that of chronic osteitis combined with uratic deposits; yet the urates are entirely absent, and the thickened tissue lies not only upon the tuberosities of the phalangeal joints but along the sheaths of the tendons and upon the sides of the bones of the fingers and toes. These nodosities are often obscurely movable, they contain no mineral matter, and in their histological structure they resemble fibromata. Yet, such may be the shape and deviation of the different joints that mere external inspection can with difficulty distinguish them from the moderately infiltrated and partially deformed articulations of chronic and torpid gout. Authors have also been somewhat divided regarding the classification of the so-called nodes of Heberden. Some have ranged them among the signs of gout, but with the majority they are considered as the result of chronic rheumatism. As an illustration of the difficulties that beset diagnosis by inspection of the affected joints, it is well to recall the fact that in certain apparently typical cases of arthritis deformans, *post-mortem* examination has revealed the previously unsuspected presence of urates infiltrating the articulations. Sometimes the little subcutaneous nodules that are so characteristic of gout are entirely absent in well-marked cases of the disease, so that their absence must not be permitted to argue too strongly in favor of the rheumatic origin of such cases. Again, it occasionally happens that, instead of attacking the smaller joints, gout invades the larger articulations with manifestations like those of chronic rheumatism.

In all these doubtful cases it becomes necessary to pass beyond the mere inspection of the affected members, and to make careful inquiry regarding the family history of the patient, his ancestors and relatives. The early life of the individual must be reviewed with reference to experience of the earlier evidences of the gouty diathesis, and the possible occurrence of premonitory or previous attacks of articular disease. The symptoms and course of such disorders must be carefully considered. The state of health during the intervals of apparent freedom from disease must also be ascertained.

In doubtful cases, Sir A. Garrod advised the examination of the blood, or of the serum of a blister, in order to determine the presence or absence of uric acid. The serum of blood that has been drawn at a distance from the seat of active inflammation is to be preferred, be-

cause urates are not found in the blood that is taken from the vicinity of an affected joint. Blood serum is also to be preferred to the serous fluid from a blister, because the latter contains a smaller number of leucocytes that might conceal the crystals of uric acid. The serum should be placed in a watch-crystal, and be acidulated with five or six drops of ordinary acetic acid. A few separate fibres of linen are then placed in the serum, and the whole is permitted to evaporate for twenty-four hours at a temperature below 70° F., until the liquid has nearly dried away. Placing the fibres under a microscope, they will be seen covered with the crystals of uric acid, if the patient be gouty. In the vast majority of cases this test will be sufficiently decisive; but occasionally the blood of a genuine gouty subject, whose joints are crippled by uratic deposits, will contain no uric acid. Again, the test cannot be expected to succeed in merely diathetic cases that have never reached the stage of articular manifestations. Bearing these facts in mind, Garrod's test may be accepted as a valuable contribution to the means of diagnosis in obscure forms of the disease.

There has been considerable debate regarding the possibility of being predisposed at the same time to gout and to rheumatism. It is a well-known fact that in the same families gout and rheumatism may follow or may alternate with each other in sucessive generations. Gouty parents may have rheumatic children, and *vice versa*. Consequently, it does not seem in the least degree improbable that both tendencies may be transmitted, say from a gouty father and a rheumatic mother, so as to be united in one or more of their offspring. It may be that in this mixed predisposition can be found the explanation of that combination of the clinical symptoms of both diseases that is sometimes witnessed. It is not improbable that many gouty subjects are patients who were originally predisposed to rheumatism, but have become gouty through improper habits of life.

The masked forms of gout often afford considerable difficulty in the matter of diagnosis. It is not in the clinical picture of the disease that obscurity lies, but in the definition of the remote cause of the symptoms. Thus it is not difficult to recognize the existence of a headache, an attack of neuralgia, a paroxysm of asthma, or an eruption of eczema; but the determination of their ultimate cause is not always easy. For those who refuse to enter upon such investigations, inquiries of this nature are without interest, and the possibility of diatheses, or predispositions to particular forms of disease, is out of the question. But for one who looks beyond the mere anatomical lesions and forms of disease into the realm of antecedent causes, nothing can exceed the importance of such researches, not only for

the sake of completing the circle of knowledge, but in order to secure information that is competent to direct the course of therapeutical endeavor. To decide as to a given case of headache or neuralgia, whether it be due to malaria, or syphilis, or an hereditary tendency to gout, is a matter of prime importance for the welfare of the patient. In like manner, the early recognition of a similar hereditary predisposition is invaluable for the proper safeguard of one who may, if neglected, become in later life the victim of confirmed articular disease. Without recognition of an hereditary diathesis, such previsions must be either impossible or destitute of a legitimate foundation.

Prognosis.

Garrod has informed us of the very significant fact that the English assurance companies always demand a higher premium for the insurance of applicants who have had articular attacks of gout than for those who have not experienced that misfortune. This is decisive as to the opinion of business men regarding the prospects of life among the gouty. Premature old age may be expected for them, and with it all the accidents to which senility is liable. Still, it is not an uncommon event to meet with individuals who have reached great age in spite of numerous articular incidents. The future of the patient will be largely determined by three things: original vigor of constitution, occupation and manner of life, and the particular mode in which the local manifestations of the disease are evolved. In very many cases, especially among those in whom the disease is an acquisition rather than an inheritance, the constitution is excellent, and it endows the patient with a power of resistance and persistence that carries him safely through many acute attacks till advanced age has been reached. This original vigor may contribute either to the safety or to the danger of the individual. If properly advised, and if sufficiently docile to conform his habits to the laws of health, such a patient may so far recover as to suffer but little during the remainder of life. But if, as is so often the case, the return of health and strength, after an attack, gives occasion to relax vigilance, and to unloose every appetite with all its pristine force, the downward course must be rapid. Feeble subjects, who have inherited weakly bodies, or have made shipwreck of an originally respectable constitution, are also liable to a rapidly progressive course of the disease.

The prognosis largely depends, also, upon the kind of life that is led by the patient. The victim of an hereditary predisposition to gout may enjoy a comfortable existence, and may reach a good old age, provided he avoids all excesses, and takes an abundance of

muscular exercise. Yet this rule has its exceptions. Such patients, sometimes, despite the neglect of every precaution, pass carelessly on through life, with but few reminders of their predisposition; while others, who observe all the precepts of wise physicians, and live with the most scrupulous regard for the laws of health, become gradually infiltrated with urates, crippled and confined to their chairs, dying miserably with dropsy and asthma, or lingering for years in a condition of hopeless wretchedness entailed by the cachexia of chronic gout.

Despite these exceptional cases, it is safe to offer a favorable prognosis when the attacks of gout are infrequent, and are limited to a single joint (great toe); when they are uncomplicated by visceral disorders, and when the general health remains good during the intervals of the disease. But, on the contrary, the future is dark for the patient who experiences frequent attacks that are separated by diminishing intervals, especially if the disease puts off its original intensity, and prolongs the duration of its crises, invading one joint after another, and ascending to the larger articulations, while the affected limbs become indolently œdematous, and remain in a state of torpid swelling for long periods of time without manifesting any very acute symptoms. Such patients have become the victims of chronic gout, and will continue in an invalid condition during the remainder of their lives. This, however, does not necessarily signify the probability of an early termination of existence. Life may endure for many years under these conditions, but recovery is not to be expected. With each succeeding attack the strength of the sufferer diminishes; the joints become infiltrated and disorganized; finally there is established a confirmed cachexia that is the result of the universal failure of function in every organ of the body. So long, however, as the heart, liver, and kidneys do not become seriously disorganized, the general health may remain tolerable, even to a late period of the disease. Careful observation of these important organs should therefore always lie at the foundation of prognosis. It should never be forgotten that in every stage of gout there is a tendency to disease of the vascular apparatus and of the kidneys. Even in the early period, before the joints have become infiltrated, while the patient is still florid and vigorous, it may sometimes be discovered that the nocturnal urine is increased in quantity, and that it contains a faint and transient trace of albumin, perhaps accompanied by a few epithelial casts. The pulse may be also tense and resistant, and the heart sounds may be accentuated beyond the normal degree of sharp definition. All these symptoms indicate a general hyperæmia or the beginning of actual inflammation in the kidneys. At a later period

these indications of vascular excitement are likely to be succeeded by the persistent discharge of urine that is irregular in quantity and of a low specific gravity, with or without the presence of albumin and casts; symptoms that are indicative of progressive interstitial nephritis. If, in addition to these changes, the sounds of the heart be muffled, or reduplicated, and the arteries show signs of atheroma in their walls, the typical morbid changes of gout are present, and the prognosis assumes the most depressing character. Uræmia, dropsy, cerebral hemorrhage, paralysis, coma, and death are among the eventualities that may be precipitated by the most insignificant accident. Even in cases that have not yet reached this degree of severity, the enfeebled condition of organs so important as the kidneys and the heart exposes the patient to a host of dangers that would under other conditions be easily evaded. A trifling bronchitis, a commonplace influenza, becomes rapidly transformed into a fatal pneumonia; or a scarcely noticeable traumatism develops into a diffuse and gangrenous inflammation. It is in such cases that the occurrence of metastasis of the articular symptoms of gout is liable to be followed by the most formidable results. In the examples of advanced visceral disease, these so-called metastases are, doubtless, sometimes the direct consequence of the visceral disorder, rather than a novel manifestation of gout; but in certain cases they are really what they seem to be, a genuine transfer of gouty manifestations from the external articulations to the internal organs of the body. The prognosis must be, therefore, largely influenced by the present condition of those internal organs. If they be in comparatively good health before the attack, revulsive measures will be frequently rewarded with success. But, if the brain, the heart, the stomach, or whatever structure is affected, be the seat of chronic morbid change, death may occur, and that with very brief delay.

Pathology.

After this protracted survey we find ourselves again facing the inquiry, "What is gout? What is the nature of that change by virtue of which uric acid and its compounds are deposited in the tissues instead of being harmlessly voided with the urine?" Gout has been defined as the most conspicuous manifestation of the arthritic diathesis. It becomes necessary to further define some of these terms before proceeding to answer the previous inquiry.

The word *diathesis* is a term that has been long employed, and then discarded from medical literature by reason of a confusion of ideas associated with its use. Differently defined by different

authors, and often vaguely employed to express various ill-known factors in the pathological field, many teachers have sought to eliminate obscurity by prohibiting the use of the word; consequently a certain amount of ill-deserved obloquy has fallen upon the term. But, properly defined and specifically employed, it does fill an important place in medical terminology; and if to all minds it fails of conveying positive information, it will nevertheless indicate a clearly comprehensible dearth of knowledge regarding particular subjects. The term may be, therefore, used as a symbol that is significant of a given amount of knowledge and also of ignorance regarding the processes of nutrition in the living body.

It is admitted that the body is constituted by the association of a vast assembly of living cells. These are brought together by an innate force that maintains them in definite relations with each other. According to the degree of perfection attained by the formative processes will be the perfection of the resulting organization. The individual constitution is, therefore, the expression of the architectural force that operates in the formation of the body; it is something that begins with the growth of the fœtal germ, and that persists till the dissolution of the organism. It consists in the orderly arrangement of the elementary parts of an organic body in accordance with the type of structure that is characteristic of the class to which it belongs. It is transmitted from parent to offspring, so that the original constitution is representative of the organization of the parental germs that have united in the impregnated ovum. But the constitution of the body may be modified by various incident causes that become operative during the course of life. A good constitution may become deteriorated by disease or injury, by starvation or poison, by disuse or fatigue. An originally feeble constitution may be invigorated and established upon a solid foundation by wholesome food, proper clothing, medication, and shelter, and by the intelligent exercise of all the organs of the body. Examples of these processes of modification are everywhere apparent. We see the vigorous and healthy youth sinking under the influence of intemperance and disease; and we are continually witnessing progress in the contrary direction from unhealthy infancy to robust and energetic manhood. All these observations serve to indicate that the constitution, though hereditary and persistent, is capable of modification in the ways of improvement or deterioration.

But the word *constitution* is properly applicable to the structure only of the body. It is necessary to find a correlative term that may be employed to express the functional activity of the organism. Such a term is furnished by the word *temperament*. Now, it is evi-

dent that in a complex structure, like the animal body, the movements of its parts will depend upon the proportion and relation of those parts to each other. According to the predominant proportion of any given part will be the predominance of the movements effected by that part. The consequent peculiarity of movement, or function as it is called in the language of physiology, marks the temperament of the individual. Hence the old terms nervous temperament, sanguine temperament, phlegmatic temperament, etc., employed to denote the predominance in the individual constitution of the nervous apparatus, of the circulatory and locomotive organs, of the fatty tissues, etc. But in the normally constituted body there is no special predominance of any given portion of the organism. With such a constitution, there is perfect harmony of action between all the organs of the body, and this fact is expressed by the phrase *normal* or *healthy temperament*.

When, however, the body is subjected to the incidence of injury or disease, great confusion of functions may arise. The constitution may be ruined; the temperament may be profoundly altered, so that it is no longer indicative of healthy physiological action. Under such circumstances, it is convenient to possess a word that may be used to signify a mode of action intermediate between physiological processes and the perversion or arrest of such functions when they have been entirely modified by disease. A descriptive term of this character is furnished by the word *diathesis*. It is in the nutritive functions of the bodily tissues that such deviations from physiological action are most conspicuous. Hence, the proper restriction of the term diathesis to those conditions of nutrition which indicate a radical departure from the normal standard of healthy function without attaining to the manifestation of those strongly marked and intensely morbid types of disease that will overwhelm the constitution if the morbid tendency be permitted to advance without check. But the essential nature of a diathesis consists not in a mere reduction of constitutional vigor that increases the predisposition to contract any and every disease that may be incident. It consists in a rearrangement of the structural units of the organism, so that there is established a predisposition to a certain disease or class of diseases. Now, such a rearrangement is an actual departure in a morbid direction away from the normal healthy standard of structure. The existence of a diathesis is, therefore, the consequence and the expression of disease. When we speak of the gouty diathesis, we speak of a condition of disease in which, though the present manifestations may be insignificant, there is a permanent tendency to greater and greater departures from health that, if unchecked, will finally result

in a paroxysmal crisis during which there are critical evacuations that give temporary relief. When we employ the broader term *arthritic diathesis*, we include the notion that there may exist a morbid condition of the body in which, under the influence of various exciting causes, a number of different disorders of nutrition may be induced. But not every disorder of nutrition may be thus excited. Only certain particular maladies can occur under such circumstances. These constitute the so-called arthritic diseases. There is not yet, however, any uniformity of belief regarding the limits of this class. Some include rheumatism, arthritis deformans, and gout in the same group; while others believe that rheumatism is an infective disease that possesses only a superficial likeness to gout, and is essentially different in its etiology and pathogeny. Arthritis deformans, also, has been similarly classified and reclassified. Other morbid manifestations, such as asthma, bronchitis, interstitial nephritis, cardiac disease, arterial sclerosis, diabetes, lithiasis, and various skin diseases, are so intimately associated with gout, either as antecedents, concomitants, or sequelæ, that they may justly be reckoned among the evidences of the gouty diathesis, really related to the culminating paroxysms that are known as gout. Hence the accuracy of the statement that the victim of gout is never thoroughly well. Inherited or acquired, the disease remains permanent, either in the diathetic or the critical form, so long as life endures. This permanence is based upon the radical change in the constitution that has been effected by faulty conditions of living, or has been inherited from a similarly vitiated ancestry. Once established, it is usually unchangeable—incurable. The graver manifestations of the disease may be often warded off by temperance and sobriety; but the less conspicuous outbreaks of the malady can be with difficulty evaded, because they are the expression of the permanent constitutional change that has been effected in the structure of the bodily organism. As Sydenham expressed it, "totum corpus est podagra."

Before proceeding to a consideration of the pathogeny of gout, it will be instructive to pass in review the opinions of some of those who have given thought to this subject. Hippocrates and his disciples taught that gout was caused by an excess of bile and other secretions that were accumulated by a morbid determination of fluids in the direction of the joints, where they produced deformity, disorganization, and painful crises. Galen accepted this doctrine, and added the observation that the disease was not so much dependent upon an alteration of the humors of the body as upon their excessive production. Essentially the same opinions were prevalent during the Middle Ages. Paracelsus and his pupils introduced the hypothesis

that the disease was not due to the excessive presence of bile and mucus, but was caused by an inflammation or fermentation within the joints, rendering the synovial fluid acid and corrosive, and causing a deposit of solid matter in and about the diseased structures. Others were of the opinion that the disease was primarily an affection of the blood which precipitated its irritating salts within the articulations of the extremities. Sydenham accepted the humoral pathology; and, if we translate into modern language the mediæval terminology which alone was at his command, we shall discover that his doctrines did not widely differ from those that are current at the present time. He believed in the existence of "peccant humors" circulating throughout the body as a consequence of "indigestion, or of impaired concoction of matters both in the parts and juices of the body." "At one and the same time the energy of the spirits (nervous energy), which are the instruments of indigestion, is diminished. The viscera are overworked, and thus the spirits, which have been long giving way, are prostrated. If it were not so, if it were a simple weakness of the spirits, children and women and the victims of long illnesses could be equally gouty. On the contrary, however, it is the hearty and robust. These it attacks only during the decline of their best and natural spirits. When this takes place, a congestion of the humors supervenes. From the two together the due concoctions are vitiated and prevented." It is very evident from these extracts that the pathological ideas of this close observer and careful reasoner were not far different from the current opinions of our own time. So long as the digestive organs remain healthy, and the energy of the nervous system continues intact, the precipitation of morbid substances from the liquids of the body cannot take place in its joints. Such, in modern phraseology, is the essential teaching of the illustrious Sydenham. These opinions exerted great influence, and were received with few dissenting voices till near the close of the eighteenth century, when, in 1784, Cullen, who was then the leader of English medical thought, announced his adhesion to the view of Stahl, who had declared himself against the humoral pathology of his predecessors. According to these authors gout was to be considered a disease of the solid tissues of the body, for there was no evidence of the existence of any morbid matters in the blood or other liquids. The articular inflammations originated de novo; and, as the joints became infiltrated only after long duration and repeated attacks of the disease, the tophi were not causes but merely the consequences of the malady. In the absence of all proof of the existence of morbid matters circulating in the blood, it was more logical to account for the occurrence of local disorders by supposing that the disease involved all the solids

of the body, and that each organ and tissue exhibited its own array of symptoms and morbid changes of structure. Neither could the heredity of gout serve as a proof of the existence of a pathological condition of the liquids of the body, because heredity consists in the transmission of the constitutional peculiarities of the parents to their children, and a "peccant humor" was certainly not a part of one's constitution. After all it was far more rational to suppose that gout was due to a perversion of the "energy of the spirits," or nervous force, mentioned by Sydenham, rather than to any purely hypothetical change in the circulating fluids of the body. In the absence of any considerable knowledge of physiological chemistry—a branch of science which had then scarcely begun to exist—it was difficult to evade the force of such criticism, and the doctrines of Cullen dominated the minds of men during the earlier years of the nineteenth century. But, with the progress of analytical chemistry, doubts arose. Some of the ablest teachers in France and England expressed the opinion that "lithic" acid was in some way closely connected with the causation of gout. Finally, in 1848, Sir Alfred Garrod furnished the conclusive proof of the presence of uric acid as one of the most essential factors in the etiology of gouty manifestations. This brilliant discovery served to re-establish the humoral theory advocated by Sydenham; and with but few exceptions the humoral pathology of gout as set forth by Garrod has been generally accepted by the modern school. The lucid simplicity with which Sir Alfred enunciated his theory of gout contributed not a little to its speedy adoption; and the recent experiments of Haig have added lustre to the name of its original expositor.

According to Sir A. Garrod the morbific substance in the blood is the sodium salt of uric acid. This circulates in the blood and lymph, and is deposited in the joints of the gouty subject, where it excites articular inflammation, by which, however, it is destroyed and eliminated in recent and sthenic cases. But the kidneys, as well as the joints, share in the disease. Hence a progressive, interstitial nephritis, beginning coincidently with the articular manifestations, or, at least, very closely following them. By reason of this renal disorder, the elimination of urates is hindered, and they accumulate in the tissues—especially in the joints; whence they are not effectually and completely removed during subsequent attacks. Hence the infiltration and disorganization of the articular structures during the advanced period of gout. Every cause, therefore, that tends to increase the production and retention of urates acts as a predisposing cause of gout. Reduction of the alkalinity of the blood, diminution of renal activity, and overloading of the tissues with nitrogenous refuse

are to be reckoned among the immediately exciting causes of the disease.

In his recent work on "Uric Acid as a Factor in the Causation of Disease" (second edition, 1894) Alexander Haig has more completely elaborated the theory advanced by Sir Alfred Garrod, and has added to it the results of a large number of experimental observations upon his own person, and upon his gouty patients. Being himself a sufferer with uric-acid headaches, he found that by giving up the use of butchers' meat the frequency and the intensity of his headaches were greatly diminished; and that they were again renewed with their original severity after a return to flesh diet. Recognizing the relationship between gout and migraine, he began to investigate the cause of these modifications in the light of gouty pathology. At first he had been, like many others, inclined to believe that such headaches must be due to the formation in the intestines of some poison—perhaps a ptomaïne—during the digestion of flesh. But the many points of resemblance between headache and gout served to awaken a suspicion that uric acid might be the exciting cause of migraine as well as of arthritic inflammation. He soon found that the symptoms of headache were invariably connected with the processes by which uric-acid compounds are circulated with the blood and are evacuated through the kidneys. During the paroxysm of headache, marked by a slow pulse of high tension, with cold extremities and skin, mental depression and disinclination for exertion of mind or body, the urine is scanty, dense, highly colored, and charged with uric-acid compounds. It is the period when uric acid is circulating in unusual quantity with the blood, and is being in similar proportion voided with the urine. It is a period of crisis, during which an inordinate surplus of uric acid is discharged from the body. The parallel between the crisis of migraine and that of gout is in this respect very closely drawn. Additional experiments soon revealed the fact that the evacuation of uric acid could be increased by the administration of alkalies, and could be diminished by the similar use of acids. Under the influence of alkalies the pulse would become full, slow, and tense, the urine would be surcharged with uric acid, and headache would be experienced. Giving medicinal doses of an acid would soon reverse the picture, the headache subsiding, and being succeeded by pricking and shooting pains in such joints as had been most actively used before the time of the experiment. The natural inference is to the effect that uric acid, which is now deficient in the blood and urine, must have been precipitated upon the tissues of the painful articulations. Here, then, is an example of an attenuated gout, induced by artificial means—a result that had been fre-

quently observed by Sir A. Garrod after the use of acid wines and beer. By these interesting experiments it is made apparent that the ingestion of substances which increase the alkalinity of the blood serves to render uric-acid compounds more soluble, and facilitates their evacuation through the kidneys; while the passage of acids into the current of the blood reduces the alkalinity of that fluid so that it cannot hold in solution the urates of the body, and they are consequently precipitated in solid form among the elements of the tissues, where they excite more or less pain—possibly active inflammation.

Pursuing this line of investigation, Haig ascertained that there can be no excess of uric acid in the blood unless there has been previous retardation of its elimination, so that accumulation has taken place within the body. He does not deny the possibility of excessive formation of the substance, but he cannot discover any satisfactory evidence of such an occurrence. He does, however, find that there is a definite ratio between the formation of urea and of uric acid, viz., uric acid : urea :: 1 : 35. When the two substances are voided with the urine in this proportion to each other, no pathological symptoms are manifested, the kidneys are merely washing out the surplus nitrogen after a normal fashion. But, if this ratio be disturbed, so that uric acid and urea are to each other in the urine as 1 : 20, for example, uric acid is present in an abnormal, pathological quantity, due, not to increased acid formation, but to the circulation and discharge of urates that had been previously detained in the tissues, where they had been formerly precipitated from the blood which has now become sufficiently alkaline to admit of their resolution and transportation to the kidneys. During this process of resolution and transportation, the surcharged blood excites the brain and nervous structures, and the patient experiences headaches, or other active symptoms, until the surplus urates have been discharged from the body, or have been, by therapeutical measures, driven out of the blood back into the tissues whence they came. We are now in a position to understand the way in which the discharge of uric acid may be modified by the daily routine of life and by the different accidents to which the individual is liable. During the cold winter weather, when perspiration is reduced to a minimum, the retention of acids that should be normally discharged through the skin serves to reduce the alkalinity of the blood and its solvent power over uric acid. Hence it follows that in bright, cold weather the blood and the urine will contain less uric acid, while its quantity will be increased in those fluids during hot weather. Consequently, uric-acid compounds may accumulate in the tissues during cold weather by reason of the over-acid condition of the blood. But with the return of

warm weather the alkalinity of the blood rises, and the circulating fluids dissolve out from the tissues the urates that were deposited during the time of cold. Circulating with the blood, on their way to the kidneys, these substances now excite the vasomotor nerves, and powerfully influence the whole vascular apparatus. In this way is effected the condition of slow, high-tension pulse, scanty urine, headache, and other symptoms that accompany a surcharge of urates in the blood and urine. But, as the spring and summer advance, the surplus urates are more or less completely washed out of the body, and a normal equilibrium is once more established. With the return of changeable autumnal weather, a new disturbance is liable to be set up. After the heat of summer, the cool weather checks perspiration, the appetite revives, and uric-acid compounds begin again to accumulate. So long as a certain degree of acidity in the blood is maintained by the absence of perspiration and by an acid-forming diet, the urates may be kept out of the blood, away from the nervous apparatus, and the patient feels cheerful, vigorous, and comfortable. But let one of the warm days of autumn excite perspiration, which perhaps is exaggerated by heavy clothing and overheated rooms—at once the alkalinity of the blood increases; it dissolves out the retained urates, and the susceptible patient experiences all the discomforts that are due to an excess of uric-acid compounds in the blood. In this way it is possible to explain many of the minor morbid symptoms that are manifested by arthritic subjects long before they ever experience any articular crises.

But it is not through the weather that these people are chiefly affected. Their diet is a matter of vital importance. In the first place, it is evident that the ingestion of acids may diminish the alkalinity of the blood. If so, the carrying power of that fluid is diminished as to urates. They are precipitated among the tissues, there to remain until the solvent power of the blood is again restored by an increase of its alkalinity. Again, the formation of acids in the alimentary canal, by reason of disturbances of digestion, may overcharge the blood with lactic acid and other substances belonging to the fatty-acid series. And, finally, the albuminous constituents of the food, with every increase of consumption, cause an increase of urea and uric acid that must be voided with the urine or be otherwise rendered harmless, if the normal alkalinity of the blood is to be maintained. In these ways the solvent power of the blood, so far as urates are concerned, is in a state of constant fluctuation. The periodical ingestion of food with every meal thus becomes a disturbing cause, so far as that solvent power is concerned. With every ordinary meal a considerable quantity of alkaline salts

is introduced into the circulation, but their effect may be either wholly or in part neutralized by the acids and acid-forming substances that are at the same time introduced as a portion of the food. Other substances also, such as iron and the metals generally, waters that contain calcic salts, opium, strychnine, the iodides, antipyrin and various coal-tar compounds, the nitrites, and certain hyposulphites, have the same power to reduce the alkalinity of the blood and to cause retention of the urates until the normal alkalinity is restored.

Undoubtedly the processes of metabolism within the tissues result in identical conditions through the formation of acids and acid salts, chlorides, sulphates, phosphates, etc., which are discharged into the blood, and there influence its degree of alkalinity. Under normal conditions, the urates in the blood are held in solution by the neutral disodic phosphate (Na_2HPO_4), which precipitates the urates into the tissues. Under such conditions the blood and the urine become poor in uric acid, but rich in acid sodium phosphate. Consequently, it is a matter of daily observation that the quantity of uric acid in the urine varies inversely as the acidity of that liquid—urinary acidity being chiefly due to the presence of acid sodium phosphate. The fluctuation of urinary acidity, therefore, serves in some degree to indicate the relative quantity of uric-acid compounds that are at any time present in the blood. This, however, is true only when the test is applied to freshly secreted urine.

As a consequence of these facts it is possible to explain the fluctuations of urinary acidity and discharge of urates that occur during each day of twenty-four hours. As night advances the urine becomes more acid. This signifies an increase in the acidity of the blood from which the urine is derived, and a corresponding reduction in the soluble urates in those liquids. But as the day progresses, and the blood is charged with the products of digestion, its alkalinity rises with various remissions dependent upon the intervals between meals, until the effects of the evening meal are dissipated during the night. Consequently, the urine is less acid by daytime than during the night; and more uric acid can be taken up into the blood and voided with the urine during the "alkaline tide" of the day than during the "acid tide" of the night. Hence the severity of hemicrania—a uric-acid headache—as the day advances, and its subsidence by night. Hence in acute gout, the incidence of articular pains and other manifestations during the "acid tide" after midnight, when the alkalinity of the blood is at its minimum, and the soluble urates that had been taken up into the blood during the preceding day are now being again discharged upon the tissues in a violent and tumultuous manner.

Passing once more in review the results of these interesting experiments and observations, it appears that the uric-acid compounds which are voided with the urine are derived: (*a*) from the nitrogenous constituents of the food; (*b*) from uric acid, urates, caffeine, or other vegetable alkaloids that have been taken, ready formed, with the food; and (*c*) from the urates that have been previously detained in the tissues by reason of their insolubility. Under normal conditions the total amount of urates formed in the body should be exactly balanced by the quantity that is discharged with the urine; and in the long run this is the fact. Urea and uric acid will then appear in the urine in the proportion of one part of uric acid to about thirty-five parts of urea, and there will be no retention of urates in the tissues, nor any morbid symptoms that can be ascribed to their accumulation in the body. If alkalies or compounds of salicylic acid be taken into the blood there will be for a day or two an excessive quantity of urates in the urine, but this excess soon subsides to the normal figure, and alkaline medication can no longer cause an increase beyond the ordinary ratio of 1:35. This fact seems to indicate that the daily formation of uric acid bears a constant relation to the formation of urea, and that, when the normal ratio in the urine is disturbed, it is owing to a fluctuation in the quantity of soluble urates in the blood. Temporary retention of urates may occur in the liver, the spleen, the joints, or other organs and tissues of the body; but, in a state of health, the quantity that is thus kept back by reason of the varying capacity of the blood is restored to the circulation so soon as the alkalescence of the blood becomes sufficient to hold in solution all the urates that it reaches. As the alkalinity of the blood is continually varying during the course of each day and night, the quantity of urates that are in circulation and that are passed into the urine is correspondingly varied; but, if reckoned day by day under normal conditions, it will be the same from day to day. As a fact, however, the daily quantity that is excreted is not uniformly the same, because of changes in the quantity and quality of the food. Uric acid may be taken ready formed in soups and gravies, or its elements may be taken in such combinations as caffeine (trimethyl xanthin) or other vegetable alkaloids. It will be then either detained for a time in the tissues until the blood can transport it to the kidneys, or it will appear in the urine in a quantity relative to urea that is above the normal ratio. In like manner, the same result will be manifested when an increase of solvent power enables the blood to take up urates that have been temporarily detained in the liver, spleen, joints, and other parts of the body.

From these considerations it is apparent that it is possible to

influence the excretion of uric acid by artificial measures. The urates that appear in the urine are directly derived from the blood, and may be assumed as the index of their quantity in the circulating fluids of the body. That quantity rises with increasing alkalinity of the blood, and falls with every decrease of such alkalescence. Every addition of an alkaline substance to the blood causes a rise of the alkaline tide; every addition of acid or acid-forming substance causes a fall in the solvent power of the blood so far as urates are concerned. Flesh food, as well as acids, wines, beer, and other acid beverages, all tend to diminish the capacity of the blood for urates, and to cause their detention in the body. Hence the accumulation of uric acid that takes place as a consequence of a highly nitrogenous diet, especially when accompanied by acid beverages that reduce the alkalinity of the blood. So long as the accumulated urates can be kept harmlessly stored in the tissues, the health of the individual does not suffer; but there is a limit to endurance, and the existence of a large deposit of uric acid in the body is a continual menace to the equilibrium of the bodily functions. A copious perspiration, or a more than ordinarily alkaline meal, or a failure of appetite through lack of exercise, may raise the alkalinity of the blood, and immediately the accumulated urates begin to dissolve and to pass into its current. If now present in excessive quantity, the circulation is disturbed by excitation of the vasomotor nerves, the arterioles contract, the pulse becomes slow and tense, the course of the blood in the capillaries is retarded, and all the functions of the body are depressed. For want of a vigorous capillary circulation the brain becomes sluggish, depressed, and irritable, causing corresponding changes in the feelings and temper of the individual. The respiration may become labored and insufficient; the heart beats slowly and laboriously; the glandular structures connected with the alimentary canal and elsewhere throughout the body receive too little blood, and become, therefore, incapable of supplying their normal secretions. The processes of digestion are correspondingly impaired. The liver, the kidneys, and the other excretory organs are all similarly hampered in function. If the store of accumulated urates be small, the difficulty is soon relieved by its discharge through the kidneys. But if the accumulation be large, and if therapeutic aid be not afforded, the embarrassment of the organism goes on increasing, until the thermogenic and nutritive functions of the tissues are released from the control of the nervous system. Local inflammation and fever may then be set up; inflammation at the point of least resistance, usually in some overtaxed joint—and fever as a consequence of general intoxication and disorder. When this tumultuous crisis has been reached, the patient is said to be suffering with articular

gout. Obviously, the disorders that lead up to this climax cannot be without symptoms; consequently every attack of gout is preceded by a long array of minor disturbances, such as headache, neuralgia, asthma, dyspnœa, palpitation, dyspepsia, lithiasis, hemorrhoids, cold feet and hands, mental depression, bad temper, etc., that are dependent upon morbid states of the circulation and a faulty nutrition throughout the body. These morbid states appear to be due to the excessive presence of urates in the blood. The final crisis is usually precipitated by some extraordinary incident that is sufficient to drive the urates out of the blood into the tissues from which they had been taken up, or into such structures as had been recently injured or overworked. Sydenham speaks of the occurrence of an unusual appetite for food as a common incident on the day preceding an explosion of gout. If, now, the gouty subject should indulge in a hearty meal of animal food washed down with copious draughts of acid wine or beer, his blood would be at once overcharged with acids and urea. Its alkalinity would be reduced, and the urates would be speedily driven out of the circulation. They would be largely deposited in such tissues as were least alkaline. Hence, after walking or other active exercise, the joints of the lower extremities—the great toe, after a dance, for example—would be the most acid of all the structures of the body, and there the urates would find lodgement. This process is most likely to occur during cold weather, when the acidity of the blood is increased through lack of perspiration. It would naturally be at its height during those hours of the day when the acidity of the blood is the greatest—that is, during the hours after midnight.

In all these particulars clinical experience agrees with theory. But when we consider the history of chronic adynamic gout, it is not so easy to follow out such an analysis. So many complications exist that the clinical picture is often blurred, and the sharp outlines of conformity with the doctrines of Garrod and Haig cannot be always continuously traced. Thus, it is frequently urged that uric acid and its compounds cannot be competent to excite such morbid disturbances in the body, because they are not poisonous, and probably exercise a merely diuretic effect, like that which is produced by urea. Ebstein and others, however, have experimentally shown that the introduction of urates into the tissues produces local irritation, especially if such salts be in a state of solution that enables them freely to penetrate the part. It must also be noted that in those who have acquired the arthritic predisposition there exists a morbid over-sensitiveness of the nervous system, and doubtless of all the tissue elements, that renders them inordinately liable to disturbance by causes that might be readily tolerated in perfect health. It is, therefore,

impossible to draw negative inferences from laboratory experiments with uric acid upon healthy subjects.

It has also been claimed that in other diseases besides gout, such as affections of the liver, lead-poisoning, enlargement of the spleen, and leukæmia, there is an excess of uric acid in the blood and in the urine without any symptoms of gouty disorder. In such cases the uric acid in the urine may rise in relation to urea to at least three times the normal ratio (1:12 instead of 1:35). But it is probable that these facts may be explained by a reference to the circumstance that in such cases the diseases are local—inflammation of the liver or of the spleen. Under such conditions the alkalinity of those organs is largely reduced, and for a long time uric-acid compounds would accumulate in them. Then, under the influence of the faulty digestion and malnutrition that is thus set up, the formation of urea and uric acid would be diminished, and the blood would become capable of transporting accumulated urates to the kidneys where they would appear in the urine greatly in excess of the urea. Any one who has had experience of chronic malarial poisoning has been able to verify in his own sensations the effect of such a surplus of urates in the circulation, producing depression of spirits, debility of mind and body, and an endless train of cachectic symptoms that speedily vanish under the influence of stated doses of a mineral acid by which urates are driven out of the blood. So long as the kidneys remain intact it is probably impossible to excite anything more than the minor symptoms of uricacidæmia, and it has not yet been shown that these are absent from the symptomatology of the diseases in question.

As for the uricacidæmia of lead-poisoning, it cannot be considered an objection to the uric-acid theory of gout, since saturnism is a well-known cause of arthritic disease; and lead operates for its production precisely like other substances that cause storage of urates in the body.

Again, it has been objected that genuine gout may occur without any trace of uric acid in the blood. But it is a well-known fact that urates are entirely absent from the blood in the vicinity of an affected joint during an arthritic crisis. Inflammation drives uric acid out of the blood, or converts it into more perfectly oxidized compounds, so that presently the entire circulation of the patient is freed from urates. Obviously, the presence or absence of uric acid in gouty blood will be determined by the proximity of an inflamed joint, by the stage of the disease, and by the degree of vigor with which excretion is performed.

The researches of Beneke, Ebstein, Bouchard, and others, referring various diseases of nutrition, such as gout, diabetes, obesity,

lithiasis, etc., to a retardation of the process of oxidation in the tissues, were supposed to throw great light upon the pathology of gout. But, while it may be true that retarded oxidation does occur in all nutritional diseases, the discovery of the fact fails to advance our knowledge. How can a mere delay of oxidation produce gout in one patient, and diabetes in another? Evidently, the cause of delay must still be sought, and we have only taken an additional step without reaching any final result. Could it be shown that uric acid is formed in excess in gouty tissues, and that urea is at the same time diminished, the hypothesis of diminished oxidation might receive a plausible support, since urea represents the more highly oxidized product. But there is no satisfactory evidence of any such disturbance of equilibrium in the formation of the two substances. The observations of Lécorché and Bouchard indicate that the amount of uric acid that is excreted by the gouty is not reduced below the normal standard. Garrod thought that the elimination of urates was less in gouty subjects than in the healthy, but he recognized the fact of fluctuation in the process. Haig has shown that the process of elimination is liable to sudden interruptions, followed soon after by compensatory increase in the opposite direction. In non-arthritic subjects these alterations serve to balance each other, but when the gouty diathesis exists there is a slight inclination in favor of accumulation of urates, so that finally the tissues are saturated, and a crisis occurs by which the system is evacuated and normal conditions are temporarily restored. In this way it is possible to reconcile the observations of Garrod and Bouchard. According to this hypothesis, it is unnecessary to postulate an increased production of uric acid, and certain experiments seem to contra-indicate such formation; hence the doctrine of retarded oxidation receives no support from the observations of Haig. He calls attention to the greater importance of a disturbance in the normal ratio between uric acid and urea in the blood, since large quantities of those substances may pass harmlessly into the urine so long as the proportion of 1 : 35 remains unchanged. It is when a considerable amount of uric acid in excess of the normal ratio appears in the circulating fluids that disorder of the bodily functions is initiated.

Undoubtedly, diminished oxidation does indirectly tend to excite various disorders of nutrition. Lack of exercise, for example, reduces the quantity of oxygen that reaches the tissues, and thus leads to their encumberment with imperfectly oxidized products of metabolism. But this alone does not excite any particular disease. We are yet ignorant of the determining causes that operate under such circumstances to produce gout in one case, obesity in another.

diabetes in a third, and so on through the list of nutritional disorders.

Such, then, is in brief the uric-acid theory of gout propounded by Sir A. Garrod, and extended by his pupil, Haig. So far as the pathological relations of uric acid with the disease are concerned, they have been very thoroughly worked out, and they serve to explain a large portion of the symptoms of the malady. But this hypothesis still leaves unexplained many of the facts connected with the initial causation of gout. Why does uric acid behave as we see it in arthritic subjects, while in other cases it is not retained, but passes harmlessly through the blood and out of the kidneys with the urine? Is uric-acid retention the real cause of the disease? The observations of Ebstein possess considerable interest in this connection. He noted the fact that uric-acid compounds are not deposited at random in healthy tissues. He observed an incipient necrosis of tissue antecedent to the deposit of urates, and expressed the opinion that without such tissue-change there could be no uratic infiltration. This, however, is merely a statement of fact, which amounts to saying that certain morbid manifestations of gout must precede the precipitation of urates—in other words, that the gouty diathesis exists before the occurrence of tangible local manifestations in the joints or elsewhere. His observations, therefore, form a contribution to the pathology of the arthritic diathesis, but do not reflect much light upon the original cause of the disease.

Of a more practical character are the opinions of Murchison and his pupils. Remarking the great disorder of digestion that frequently accompanies an attack of gout, and noting the resemblance between many of the symptoms of gouty dyspepsia and the disturbances that follow upon derangement of the liver, they referred the initial morbid process in gout to that organ. They supposed that the formation of urea is chiefly accomplished in the liver, and they inferred that the presence of an excess of uric acid in the blood and elsewhere must be due to imperfect oxidation of nitrogenous alimentary substances in the hepatic cells. In this way a surplus of uric acid is turned loose upon the circulation, and the phenomena of uricacidæmia soon appear. It is very true that in certain congestive conditions and chronic inflammations of the liver there is an increase of urates in the urine; but uratic deposits in the joints or elsewhere never occur in such cases; and besides there are many gouty subjects who rarely, if ever, exhibit any evidence of serious hepatic disturbance. The corner-stone of this theory is, moreover, not well founded. The liver cannot be regarded as the principal agent in the formation of urea. It is probable that urea, with other nitrogenous refuse, is formed

throughout the body, wherever protoplasm is undergoing oxidation. It is gathered up from all the tissues, and is carried to the kidneys for final ejection from the system. Consequently it is improper to speak of the disturbance of relation between the formation of urea and uric acid as a result of hepatic disease alone. If such defective oxidation does actually occur, it is the consequence of a general disorder of metabolism—in other words, it is dependent upon the existence of the arthritic diathesis. In the general deterioration of function that is characteristic of the diathetic condition, the liver shares; but its disorders are not the prime cause nor the only source of gout. They are a part of the evidence of universal degradation and reversion toward inferior types of organization.

In like manner, the existence of a plethoric condition of the organism has been regarded as the cause of gout. Because many arthritic patients are florid and robust, it has been thought that gout was due to an excessive function of the blood-making organs. But there are many gouty patients who are thin and comparatively ill-nourished, and many other people, though full of red blood, never experience any gouty symptoms. Still it is true that great energy of the nutritive functions does often favor the genesis of the malady. The absorption of large quantities of acidulated alcoholic beverages causes an excessive irrigation of the tissues—in short, a dilution of their protoplasmic basis. In this way, certain metabolic processes may be either hindered or accelerated. The alcohols, and especially the ethers, that are thus introduced, undoubtedly exercise a certain inhibitory influence over the metamorphosis of molecular structure, by their presence alone causing an arrest of oxidation, or at least a retardation of that process, analogous to what has been recently observed by Professor Dewar in connection with the phenomena of fluorescence and phosphorescence. The excessive distention of the stomach, the overtasked condition of the intestinal glands, and the final failure of digestive power, all combine to modify the entire process of assimilation and nutrition. In the quantity and quality of the food, in the character of the digestive process viewed in the broadest sense of the term, may be founded the first beginnings of morbid function which, aided by all the secondary causes that act upon the constitution, finally result in a permanent alteration of structure, constituting what is known as the gouty diathesis. Upon this pathological foundation, under the influence of bad hygienic conditions, excessive labor, fatigue of mind and body, lack of exercise, traumatism, debauchery, and everything that tends to depress the sum of vital energy, may be developed the maladies that are allied with gout, or the various disorders that culminate in the articular manifestations which are the

most conspicuous evidence of arthritism. It is not improbable that the aromatic sulphates, which are formed in the small intestine, and are increased in quantity by various disorders of digestion, may contribute to the disturbance of uric-acid equilibrium during their passage through the blood on the way to the kidneys. Haig has shown that the presence of inorganic sulphuric acid salts diminishes the alkalinity of the blood, and thus causes temporary retention of uric acid. It is not unreasonable to suppose that the organic sulphates may act in a similar manner; but this subject needs additional investigation. There can be, however, no reason to doubt that from the decomposing contents of an unhealthy intestine many poisonous compounds find their way into the blood and are carried to the tissues, where they profoundly influence the process of metabolism. Unfortunately, however, we are not yet able to trace all the steps in the chemistry of the cell by which molecular exchanges may be effected, retarded, or accelerated.

The important researches of Sir William Roberts on the chemistry of uric acid in gout have thrown some light upon the nature of the changes that occur during the process of uratic infiltration of the tissues ("Uric Acid, Gravel, and Gout," 1892). Having shown that the urates in gouty joints consist chiefly of an almost insoluble sodium bi-urate, while in the serum of the blood, and in other similar alkaline fluids, uric acid enters into combination as a soluble quadri-urate, he concludes "that in the normal state uric acid is primarily taken up in the system as quadri-urate, and that it is finally voided with the urine as a quadri-urate. In perfect health the elimination of the quadri-urate proceeds with sufficient speed and completeness to prevent any undue detention of it in the blood. But in the gouty state this tranquil process is interrupted, either from deficient action of the kidneys or from excessive introduction of urates into the circulation or from some other cause, and the quadri-urate lingers unduly in the blood and accumulates therein. The detained quadri-urate, circulating in a medium which is rich in sodium carbonate, gradually takes up an additional atom of base and is thereby transformed into bi-urate. This transformation alters the physiological problem. The uric acid, or rather a portion of it, circulates no longer as the more soluble and presumably easily secreted quadri-urate, but as bi-urate, which is less soluble, and probably also—either for that reason or because it is a compound foreign to the normal economy—less easy of removal by the kidneys. The bi-urate thus produced exists at first in the gelatinous (soluble) modification, but with the lapse of time and increasing accumulation it passes on into the almost insoluble crystalline condition, and then precipitation becomes

imminent, or actually takes place." Sir William Roberts then shows that these changes are accelerated by the increase of uric acid in the solvent medium, and goes on to say:

"Assuming that the inflammatory arthritic attacks in gout are directly due to copious and sudden precipitation of crystalline stars and needles of sodic bi-urate in the cartilages and fibrous structures of the joints, the evidence before me indicates that such copious sudden precipitation can only take place when the fluids bathing these structures are impregnated with uric acid in at least the proportion of 1 part in 2,500. Below this point the precipitation occurs slowly and scantily and only in the form of short scattered needles. . . . It is quite conceivable that this slighter precipitation in the tissues of short scattered needles might account for certain irritations in the various organs, such as characterize irregular or larval gout; but it could scarcely engender downright inflammatory attacks. It is further conceivable that the presence in the blood of such scattered needles might constitute foci around which clotting might take place, and that the thrombosis not infrequently observed in gouty cases might thus be accounted for. The impregnation of the blood in gouty persons with uric acid to the extent of these lesser degrees is within the range of observed actualities."

Sir William further shows that the precipitation of urates is facilitated by the addition of sodium salts to the solution, and by reduction of the temperature. In this way he explains the more frequent deposit of urates in the joints of the feet rather than in the deeper and warmer regions of the body, since it appears, from analysis, that the synovia and articular cartilages contain a larger percentage of sodium salts than exists in any other tissue (*loc. cit.*, p. 103). In this result of laboratory experiments Roberts and Haig are at variance, for Haig claims that uric acid is more soluble in alkaline fluids containing di-sodic phosphate than in those which contain the acid sodium phosphate. Probably, however, the presence of sodium salts that furnish the base for sodium urates is the important fact in the case.

The author then proceeds to show that it is possible in the joints of dead animals to produce a uratic infiltration of the cartilage that shall exactly counterfeit the deposits in a gouty articulation (*loc. cit.*, p. 105.)

"Tarsal bones of a pig were suspended in wide-mouthed phials charged with a saturated solution of bi-urate made in hot water and then cooled. The phials were chloroformed, corked, and placed in the warm chamber or at the temperature of the room. Re-precipitation of the bi-urates takes place in two or three days. If the bones are

now examined, the articulating ends are found to be encrusted with a chalky matter which cannot be wiped off with a towel or removed with a nail-brush. If vertical sections of such cartilages are examined with the microscope, the deposit is seen to be situated in the substance of the tissue, close beneath the synovial surface of the cartilage, and to be composed of a dense felt of fine needles of biurate." This deposit is supposed to occur as an infiltration from the synovial fluid rather than as a result of any primary morbid changes in the cartilages. In this particular Roberts and Ebstein, therefore, are not agreed.

Roberts also proceeds to explain the superior tendency of synovia to thus deposit urates by stating that the fluid is especially rich in sodium salts which favor the precipitation of uric acid, and that the isolation and stagnation of the articular contents may be supposed to aid the process. In this connection he quotes an observation made by Frerichs, who found that "stall-fed horses and oxen, leading an idle existence, had twice as much synovia in their joints as similar animals roaming in the meadows or doing work. . . . In the idle animals the synovia was more watery and contained less albuminoid matters, but, and this is significant, a larger proportion of mineral salts, which consist almost entirely of sodium salts. We might conjecture from this fact that if horses and oxen were liable to uratic precipitations, the idle stall-fed animals would be more subject to such deposits than the same animals leading a more active life. Perhaps we may discern herein one reason why men who lead a sedentary life are more subject to gouty deposits than men who take active exercise."

As for the uratic deposits in the joints, Sir William Roberts considers them as not necessarily permanent. He agrees with those who teach that they may sometimes exist in the articulations without exciting the manifestations of gout; and, conversely, attacks of acute articular gout may occur without any uratic deposits discoverable after death. When urates are slowly and moderately precipitated, the first of these conditions obtains; when long intervals of health succeed the articular crises, the second condition may result from the gradual solution and removal of the deposit. He is also of the opinion that the phenomena of articular inflammation are for the most part the consequences of mechanical injury caused by the presence of the infiltrated salts. He cannot admit any poisonous effects from uric acid or its salts, and is therefore inclined to suppose that in the irregular forms of gout there is really an overlooked precipitation of urates in different parts of the body, where they excite disorder by mechanical interference with the function of the affected structure.

That this is not an improbable hypothesis is shown by the fact that the blood-serum in gouty subjects is often supersaturated with sodium bi-urate, so that precipitation into the tissues may be very easily occasioned.

In this learned exposition of the chemistry of the urates its author has made an invaluable contribution to science; but with the exception of the demonstration of the different states of combination into which uric acid may enter, he adds very little to our knowledge of the pathogeny of gout. With the witty German professor we may say, after reading these interesting lectures, that gout seems to consist in the excessive facility with which quadri-urates are transformed into bi-urates. But whence this morbid facility? The question remains unanswered.

Profoundly impressed with the difficulties that attend a purely humoral theory of gout, Cullen and many of his followers, more recently Sir Dyce Duckworth, have sought in the nervous system a controlling influence over the manifestations of the disease. The effects of mental fatigue and violent nervous disturbance in the determination of an attack, the well-known nervous perturbations that accompany inflammation of the joints, the fugitive and migratory character of the phenomena, the intimate connection between certain arthropathies and morbid states of the central nervous system, as in tabes dorsalis, all seem to indicate that gout, if not a nervous disease, is most profoundly influenced by nervous action. A kindred disorder —arthritis deformans—has often been conjectured to be the consequence of perverted nervous influences. If so, why may not gout, also, be a reflection of cerebro-spinal derangement?

It is undoubtedly true that the nervous system does intervene most actively in all the phenomena of acute gout. Its functions are radically modified during the course of chronic, senile gout. But if we meditate upon the incipiency of the malady, as it is developed in previously healthy subjects without antecedent heredity, we shall discover that the nervous symptoms are secondary to the action of morbid causes from without. It is the unfavorable climate, the deficient exercise, the luxurious diet, the special beverage, that is in evidence long before the manifestation of any morbid nervous phenomena. But when the gouty constitution already exists, either as an inheritance or as an original acquisition, every function is liable to derangement, and the signs of diathetic disorder may be traced in every organ and function. A vicious circle is thus established, so that disturbance in one function excites disorder in another. The nervous system intervenes as a bond of communication between the various structures of the body, and opens its paths for the distribu-

tion of morbid movement, somewhat as the circulating fluids serve to convey morbid matter to every part of the organism. Of any more radical or efficient participation of the nervous apparatus in the genesis of gout, there is no satisfactory evidence.

Quite recently, Rachford, of Cincinnati, has made a number of interesting observations (*Medical News*, May 26th and Nov. 3d, 1894) on the action of paraxanthin as a factor in the etiology of migraine. He confirms the results obtained by Haig in similar cases, regarding the increased excretion of uric acid compounds in connection with the paroxysms of headache or epileptiform convulsions that sometimes replace the headache. He also finds that coincidently with this evacuation of urates there is a decided increase of paraxanthin in the urine. This incompletely oxidized nitrogenous compound is present in an almost infinitesimal quantity in ordinary urine; but, in cases of migraine and migrainous epilepsy, it and the other leucomaïnes of the xanthin group are discoverable in relatively large quantities in the urine. According to Salomon, one litre of healthy urine contains only one milligramme of paraxanthin; while from the same quantity voided at the time of a migrainous epileptic attack, Bange and Rachford, employing the method of Salkowski and Salomon, obtained a cubic centimetre of the substance in the form of a highly concentrated solution giving all the reactions of paraxanthin. One minim of this solution injected into the peritoneal cavity of a full-grown mouse produced great exaggeration of reflex excitability. This was followed in two minutes by tetanic contraction of all the muscles, which continued almost without intermission for three hours, until death occurred. From these experiments it is evident that, although uric-acid compounds are not poisonous, they may be accompanied by other kindred substances that are intensely lethal. Haig and Bouchard have demonstrated the excessive presence of urates in the aggregate urine that is discharged during and after the attack of gout. Haig has also made clear the gouty affinities of hemicrania. This additional research of Rachford shows that the other nitrogenous excreta of the uric-acid group are simultaneously increased when urates are redundant in the urine. Taking into consideration their intensely poisonous character, it seems not improbable that they may exert considerable influence in determining the symptoms of the arthritic crisis. At any rate, these experiments serve to indicate the path to be followed in future researches into the physiological chemistry of gout.

We are therefore, at the conclusion of this widely extended survey, brought to a conception of gout as a fundamental derangement of the constitution, that may be either inherited, or acquired

through a persistent course of insufficient muscular exercise, gluttony, and intoxication with highly acidulated alcoholic and etherealized beverages, causing disorder of digestion, assimilation, anabolism, and elimination, with all their attendant train of morbid symptoms, accompanied by a deposit of solidified urates infiltrating the tissues in and near the joints, culminating in violent nervous crises connected with articular inflammation, and tending to the final establishment of permanent disease, principally involving throughout the entire body the organs of locomotion, circulation, and excretion.

Treatment.

Hygienic and Prophylactic.

Since gout is a constitutional disorder of nutrition that is either inherited or acquired, and since it exists as a diathesis in which are manifested intermittent paroxysmal attacks that may finally become merged in the phenomena of chronic gout, it follows that the treatment must be preventive when there is danger that the constitution may be undermined; it must be constitutional and general when dealing with the diathesis; and special and local during acute attacks. Chronic gout requires a combination of general and topical medication, together with careful observation of hygienic regulations. The range of therapy in this disease is, therefore, exceedingly wide and comprehensive. There is no room for doubt regarding the advantages to be derived from properly directed treatment, even though it be admitted that, once acquired, the gouty diathesis is permanent. Many incurable disorders are among those that offer the greatest opportunity for the exhibition of therapeutical skill in the relief of suffering and the prolongation of life. It is also all important to guide the heirs of an arthritic inheritance in a way that shall minimize the consequences of ancestral misfortune. If their constitutional predispositions are thoroughly comprehended, the transient maladies which they may experience can be more safely and speedily conducted to a successful conclusion than if they are subjected to a treatment without reference to their diathetic peculiarities. And when the frightful suffering of an articular crisis is experienced, even the most obdurate sceptic must admit the necessity for anodyne measures, because no patient under such circumstances can be persuaded to find comfort in scientific explanations of the self-limited and curative nature of the spontaneous evacuations that constitute the principal phenomena of the attack. By judicious aid afforded during the paroxysms much subsequent disorder may be averted, and the return of these paroxysms may be prevented or at least may be longer post-

poned, especially if medical treatment be reinforced by efficient hygienic measures during the intervals of apparent health. Of the highest importance is a due recognition of the fact that gout is not an occasionally recurring malady that consists merely of certain articular manifestations of an inflammatory character. This is the narrow view of the uninstructed laity, and it is one of the principal obstacles to prophylactic and hygienic treatment. Hence the importance of instruction as well as medication; for these people must be made to understand that the disease is not seated in their joints only, but that it is an affection of the entire organism, and that it will inevitably lead to serious, if not fatal, disorder of the vital organs of the body unless restrained by wholesome living and a wisely directed therapy. By such far-seeing providence it will be often possible to rescue men who would be otherwise totally wrecked before their time.

In order to carry into effect a rational system of prophylaxis it is necessary to recognize the existence of the arthritic diathesis, and to comprehend the fact that by reason of its establishment through inheritance or acquisition, the processes of nutrition are modified in a way that leads to intoxication and encumberment of the organism with imperfectly oxidized nitrogenous compounds that are chiefly derived from the food. Since in the majority of cases the diathesis is inherited, it is important to begin at the earliest age with the children of arthritic families, and to enforce through life such hygienic rules as are calculated to obviate the tendencies that grow out of the working of a defective constitution. From earliest infancy the child should be accustomed to the open air, and should be reared in a dry and sunny yet cool and bracing climate. The vast interior of the continental masses of land in the northern hemisphere, and the highlands of South America and northern Africa, afford the nearest approximation to these conditions. For the inhabitants of damp and chilly sea-coasts, a removal, at least during the unfavorable seasons of the year, to a more favored region should be advised. In addition to the ordinary athletic sports in the open air, horseback exercise should be practised by the growing child as soon as he can hold himself upon the saddle. The functions of the skin must be promoted by daily baths, and by the use of friction with coarse towels, brushes, hair-mittens, and the like. The diet must be regulated so as to avoid excess of all kinds. Sweets and lean meat are to be used with great moderation. Every child should be taught to like milk, and to drink it in considerable quantity, since no other article of food exerts so great an inhibitory influence over the formation of intestinal toxins. Tea and coffee, tobacco and alcohol must never be allowed to the growing child or youth, since they all serve

to retard the processes of metabolism and oxidation in the tissues upon which the healthy liberation of bodily force is dependent. It may seem superfluous to advise a very moderate course of study in the intellectual training of such children, but it is among that class, precisely, that restraint rather than stimulation is needed, for it is in the foremost families, and within the circle of the bright and active members of society, that these precautions are most needed. A broad and comprehensive education, including a knowledge of the laws of health, and the cultivation of a habit of self-restraint, should be preferred to the miserable system of cramming for examinations that is now generally practised in our public schools and universities as the ideal method of preparation for the labor and responsibility of public life.

Diet.

A similar course should be prescribed in all cases where there is danger that a healthy individual may become arthritic. Unfortunately, however, the physician is seldom consulted until the diathesis has been acquired. It then becomes necessary to regulate the diet of the patient, in order to obviate, so far as possible, the minor accidents that precede the occurrence of articular inflammation, and to prevent the deposit of urates in the joints or elsewhere. If the patient be tractable, much can be done to postpone, if not actually to abort, the crises that otherwise would be precipitated by an injudicious regimen.

Since a large part of the injury that is effected during the course of gout is due to an excess of urates in the system, and since the etiology of the disease is closely connected with the formation and circulation of imperfectly oxidized nitrogenous compounds, it is expedient to limit the ingestion of alimentary substances that are rich in nitrogen. In order to facilitate this arrangement, Sir W. Roberts has constructed the following table that shows at a glance the average percentage of albuminous substances contained in different articles of food:

Animal Food.	Albuminoid matter.
Butcher's meat	19 per cent.
Fowl	20 "
Game	22 "
Fish	17 "
Eggs	13 "
Milk	4 "
Cheese	30 "

Vegetable Food.	Albuminoid matter.
Bread	8 per cent.
Oatmeal	12 "
Rice	6 "
Green peas	6 "
Potatoes	2 "
Carrots, turnips	1 to 2 "
Green vegetables & salads,	1 " 2 "
Fresh fruit (excluding nuts)	0.5 " 1 "

In making use of such a table it is necessary to take into account the relative quantities of these articles as they are usually eaten. Thus cheese, which contains 30 per cent. of nitrogenous matter, may be very harmless when taken in small quantity as a relish, though quite as injurious as butcher's meat if consumed in corresponding amount. In the same way it may be perfectly safe to use a little meat, though wholly unwise to take it in any considerable quantity. Haig has shown in his own person the great advantage of leaving off the use of butcher's meat in cases of hemicrania. In the work which has been referred to above he says: "Having been all my life a sufferer from migraine it was in the autumn of 1882 that in despair of obtaining any complete relief from drugs, and not without some fear that I was really suffering from organic disease, I gave up all butcher's meat and replaced it by milk and fish.

"I had previously tried a great variety of alterations in diet, including an increased allowance of meat and various alterations in quantity and quality of less important constituents, such as sugar, tea, coffee, and tobacco, without any noticeable result. But on the non-meat diet a change was at once apparent; my headaches diminished both in frequency and severity, and from an average of one a week they fell steadily as the diet was persevered in, down to one in a month, one in three, six, eight, or twelve months, and eventually eighteen months elapsed without an attack of notable severity."

As a control-experiment the author found that a few meals of meat and wine would at any time reproduce his headaches in all their pristine severity.

Now we know that migraine is one of those disorders that are usually symptomatic of the arthritic diathesis; hence the great value of this experience—which, by the way, is not uncommon—as indicative of the proper method of prophylaxis whenever the predisposition to gouty disorders exists.

It is claimed by many authors that abstinence from meat is not expedient in all cases, and some have gone so far as to advise the contrary regimen, forbidding the consumption of sugar and starch, and enjoining the use of animal food almost altogether. It is urged by these teachers that many persons are unable to live without meat, and that a vegetable diet causes severe dyspepsia, accompanied by flatulence, acid eructations, and various other disorders that are obviated by an almost exclusively animal diet. Among the laity it is common to encounter a prejudice against the use of milk as an article of food, because, as they say, "it makes me bilious." Now, there is for all these opinions a certain foundation of fact. It is true that for the majority of people a mixed diet is desirable. But, when

called upon to deal with an individual who is predisposed to arthritic diseases, we are brought in contact with a morbid constitution, and frequently with a depraved appetite and retarded nutrition. Haig has shown that under such circumstances animal food gives present relief at the expense of future suffering. We find such patients eager for "strong food," and soon suffering if they do not have it, but also tormented at intervals by "sick headaches," bilious attacks, etc., until an articular crisis clears their pathological atmosphere. Those same patients, however, if gradually accustomed to a milk, cereal, and vegetable diet, will lose their craving for animal food, and will find themselves relieved of their voracious appetites and also of their dyspepsia and other disorders. There are very few patients who cannot learn to take milk to their great advantage, if they will consent to begin with small quantities—a spoonful with each meal, or every hour or two, as the case may require—followed by a daily increase of the amount until it can be taken with perfect freedom.

Particularly useful is milk in all cases of intestinal fermentation, for it has been shown that a milk diet causes great reduction of the hydrogen-ethereal sulphates that are formed in the intestine and are discharged with the urine. The same thing is true of the toxic compounds of the xanthin class. Consequently it is important to form the habit of depending largely on milk as an article of diet in these cases. The patient should be instructed that his "biliousness" is the result of disease, and not a consequence of drinking milk. He should also be encouraged by the information that the constipation which first follows such diet will in the course of a few weeks be cured by the milk itself. In this way all but a very few can be taught and benefited. Occasionally, some remarkable idiosyncrasies relative to milk will be encountered, in the form of urticarious rashes, and their like, whenever it is tasted, even in the smallest quantity. An exclusively milk diet must not be prescribed for patients who are leading an active life of muscular exertion. For them a variety of food is needful, and a certain amount of meat is essential to the accomplishment of really hard work. Fortunately, however, gout is rare among this class of laborers, unless, like the London 'longshoremen, they consume excessivee quantitis of porter, thus overloading their tissues with unnecessary nutriment. Herein lies the kernel of the whole matter: avoid all excess in eating and drinking. When a patient gorges himself every day of his life upon appetizing viands selected from a vast and varied diet-list, any kind of restriction will prove beneficial. Such people, for the reasons specified by Haig, usually find it easier to give up vegetables rather than savory meats. Both together have been too much, but upon meat alone they begin to feel

an improvement. Yet for many this is only a temporary relief, and after a time the old nitrogenous encumberment reappears. Far safer is the position of one who can surrender flesh food, nourishing himself upon milk and vegetables. He may experience more discomfort at first, but soon his morbid craving for nitrogenous substances will subside, his acid dyspepsia will gradually disappear, cardiac intermission and irregularity will be arrested, neuralgia and headache will cease or be greatly relieved, despondency will give way to cheerfulness, and the intellectual functions will acquire a degree of lucidity to which the patient has been long a stranger. Such people have been over-fed; the reduction of the quantity they consume is the thing of prime importance, and at first it matters little whether they abandon flesh or the saccharine and starchy elements of their over-abundant diet. In the long run, however, they will be the better for a non-nitrogenous regimen. The learning and skill of the physician will find ample opportunity for display in the guidance of these patients to the adoption of a diet that is suited to their condition and necessities. In the vast majority of cases it will be found that after a few weeks dyspeptic subjects, who, on a full diet, were continually complaining of their inability to tolerate fruits and vegetables, will now have no difficulty in digesting such substances, to their great advantage in the matter of constipation, hemorrhoidal attacks, and other kindred complications. Sir A. Garrod has shown the utility of a vegetable diet as a source of hippuric and benzoic acids which act as solvents of uric-acid compounds. By varying the food of a patient it will be found that upon a flesh diet the urine becomes charged with urates, and it deposits free uric acid when cooled. If he is fed with vegetables and cold water, the uric acid compounds quickly disappear, and are replaced by hippuric acid. Led by considerations of this sort, and confirmed by his own fortunate experience, Haig has prepared the following diet-table which will be found generally useful in cases of predisposition to arthritic disorders. It is also of great value for the guidance of elderly people who, though not actually gouty, are subject to hemicrania, neuralgia, and other kindred affections.

"*Breakfast.*—A large soup-plate half-full of porridge, eaten with milk, and salted.

"A few mouthfuls of eggs, prepared in various ways; or some mushrooms, tomatoes, or other vegetables, and occasionally fish.

"One or two rounds of bread, or its equivalent in toast or scones, with plenty of butter.

"A cup of milk (previously boiled) flavored with tea, coffee, or cocoa.

"Finish with a small quantity of any fruit that is in season.

"*Lunch.*—Potato and one other vegetable, cooked in various ways (a plain boiled potato, the summit of ordinary English vegetable cookery, I never have on my table; my cook has been educated to better things than that), eaten with butter, fat, or various sauces.

"Pudding, tart, or stewed fruit.

"Biscuit and butter, with cheese. (Biscuit, bread and breadstuffs are taken in considerable quantity, not a mere mouthful or two, as is often the case with meat-eaters; and those who attempt to reduce their meat without increasing their breadstuffs are likely to get into difficulties.)

"A little fruit as at breakfast.

"For drink, a little milk, which in winter is often warm; or water, often taken, in summer, with a little fruit syrup, such as Stower's Lime-Juice Cordial.

"*Afternoon Tea.*—Bread and butter and cake of various kinds. A little milk and water flavored with tea.

"*Dinner.*—Soup made without meat stock. (See recipes in 'Maigre Cookery,' by Sidney Lear; London, Rivingtons.)

"Fish or an egg, or a small bit of meat is occasionally substituted for these.

"Two vegetables, with sauces, butter, or fat.

"Any ordinary pudding, tart, or stewed fruit.

"Biscuit and butter, and perhaps cheese, if the quantity of fish or egg has been small.

"A good supply of various fruits for dessert.

"For drink, water with fruit syrup, aerated waters, or a little milk, which I often take warm in winter.

"A tumbler of water, aerated water, or in winter hot water at bedtime.

"It is not necessary to interfere with established habits as to wine, beer, or spirits, unless they are obviously doing harm, for once the introduction and formation of urates (and nitrogenous toxines) has been reduced, the effects of these beverages in preventing elimination may almost be neglected."

During early life the subject of the arthritic diathesis can usually enjoy great latitude in the use of fruits, but, as the years advance, and the tendency to gouty disorder becomes more pronounced, many patients grow intolerant of the vegetable acids. For such people it is unsafe to eat currants, gooseberries, grapes, tomatoes, and other fruits or vegetables that are rich in acid. When the tissues are charged with nitrogenous poisons, a slight indulgence in acid fruits or drinks may be sufficient to cause pain in certain joints, headache,

dyspepsia, and other premonitory symptoms of a gouty attack. Still, it is a noteworthy fact that individual idiosyncrasies are so variable that many persons can with impunity tolerate what would be almost poisonous to others.

The use of sugar has been greatly decried, but here again there is no evidence that it is directly injurious. Only when it is taken as part of an excessive diet is it harmful by furnishing fermentable matter to the contents of the stomach and intestines. Especially when associated with alcohol in wines and malt liquors it is likely to add to the acidity and flatulence that render the patient so uncomfortable. It is thus that cider and similar drinks may be harmful. Vinegar, pickles, salads, and similar articles in which acids, starches, and sometimes sugars are combined, are generally productive of injury and discomfort.

The question of beverages is one of the most important matters for consideration in this connection. It is one of the oldest observations that water-drinkers seldom suffer with gout. The passage of water through the tissues promotes interstitial oxidation, and assists in the removal of refuse matters that are delayed on their way to the kidneys. A number of experimenters have noted an increase in the quantity of urea in the urine after copious draughts of pure water. When gravel is associated with gout, the effect of waters which are almost chemically pure, like that of the Poland Spring in Maine, is sometimes quite remarkable. Patients who drink freely of such water are often rewarded by an abundant discharge of sand and gravel with the urine, followed by complete relief from preceding uneasiness in the region of the kidneys. When such spring waters cannot be obtained, an excellent substitute may be found in the distilled water from which artificial ice is made, or even in the condensed steam from an engine boiler. The temperature of the water that is drunk should be determined by the object in view. When simple diuresis is desired, the beverage should be cold; but if it be desirable to quicken the action of the skin, and to stimulate a feeble circulation, hot drinks are to be preferred. In winter especially, and when the digestive functions are debilitated, the effect of warmth is desirable in order to avoid the temporary arrest of gastric secretion that follows a cold draught.

Alcoholic beverages do not exert any appreciable influence upon the development of the gouty diathesis unless taken in the form of wine or malt liquors. Sir William Roberts has shown that the addition of alcohol to the liquid in which sodium bi-urate is held is without effect upon the solubility of the salt, or influence of any kind in the way of accelerating or retarding its precipitation. It is, more-

over, a matter of common observation that distilled spirits are consumed in large quantities by whole races of men who never become gouty.

But the consumption of wine and malt liquors, if conjoined with abundant nitrogenous aliment, does seem to favor the occurrence of arthritic disorders. Now, these beverages differ from spirits chiefly in the fact that they contain various saccharine substances, acids, and a certain amount of ether due to the action of acid upon the alcohol that they contain. Beer contains acids in a comparatively small quantity, but, when consumed in the enormous draughts that are common among the votaries of Gambrinus, the amount of acid that is introduced into the body may be very considerable. In this way the accumulation of urates and other nitrogenous refuse is aided. The ethers, also, which give odor and flavor to wines are not without influence upon the processes of oxidation in the tissues to which they are carried. According to Bence Jones, the various wines in common use may be ranked in the order of their acidity, beginning with the lowest: Sherry, port, champagne, claret, madeira, burgundy, Rhine wine and Moselle. Haig declares as the result of his analysis that "Champagne is about the most acid of wines, and the cheaper beers are generally more acid than those of better quality. I found acidity equivalent to 18 grs. of oxalic acid in a pint of 4d. ale, and 25 grs. in a pint of stout. Sherry, 37 grs. in a pint. Port about the same. Claret, 46 grs. to the pint, and champagne, 49 grs. to the pint." According to Sir A. Garrod: "The least acid of all alcoholic fluids are Geneva and whiskey."

Haig is however quite positive that the ordinary use of alcoholic beverages is innocuous as regards the development of gout, provided that the blood and the tissues be kept clear of nitrogenous refuse through the adoption of a properly regulated diet. In all cases such drinks should be largely diluted with water. Sydenham counselled such dilution of the strong ales affected by his countrymen. The French also always practise a similar attenuation of their light wines. The famous Erasmus appears in his letters to have thought differently of the matter, and he died miserably of gout and stone in the bladder.

The non-alcoholic beverages, tea, coffee, and chocolate, are tolerated with difficulty by the arthritic constitution. Many patients suffer severely with migraine so long as they indulge in the use of these drinks with their meals. This is due in part to the caffeine—a nitrogenous substance—which they introduce into the tissues, and in part, as Haig has shown by experiment, to the accumulation under their influence of urates and other nitrogenous matters in the body. Caf-

feine is said to retard the processes of metabolism, hence its unfavorable influence in all cases where metabolism needs acceleration.

We are thus brought back to the beverages of childhood—milk and water—as the only liquids that are fitted for the harmless irrigation of the tissues. Especially true is this when the organization of those tissues is modified or in danger of modification through the influence of hereditary causes or acquired habits of excess in the matter of eating and drinking.

By a careful modification of the diet upon the principles that have been thus indicated, it is possible to reduce very considerably the nitrogenous refuse of the body. Haig ascertained, as a result of repeated observations, that while on ordinary food his daily excretion of urea was from five hundred to six hundred grains *per diem*, it was reduced to about three hundred and fifty grains after the adoption of a restricted diet. Finding also that under all circumstances the production of uric acid bears to urea the ratio of 1 : 33 or 1 : 35 there must be a corresponding reduction of the less oxidized compounds of nitrogen. There will therefore be less opportunity for the accumulation of those substances in the tissues and less chance of the consequent occurrence of nitrogenous poisoning.

Exercise.

The whole process of interstitial oxidation can be farther facilitated by exercise in the open air which serves to increase the respiration and to favor the absorption of oxygen by which it may be possible to increase in some degree the amount of urea at the expense of uric acid and the other incompletely oxidized compounds of nitrogen. It is, however, still an open question whether muscular exercise does actually disturb the ratio between urea and the other nitrogenous compounds by promoting their oxidation into urea, or whether the undoubtedly good effects of manual labor, gymnastics, and other methods of promoting muscular contraction are due to anything more than the improvement in excretion that follows such exertions. It is certain that the exchanges in muscular tissue are greatly increased by use, and that the excretion of refuse products from such tissues is also accelerated in a corresponding degree, thus affording opportunities for the introduction of fresh supplies of nutriment and for the liberation of the energy that they incorporate with the substance of the organism. But when the gouty diathesis has been fully established it becomes necessary with regard to all forms of muscular exertion to practise the same moderation that is advisable in the matter of diet. Excessive labor and unusual exercises may serve to precipitate an attack of gout if the

predisposition be fully developed. In this respect exercise may produce a result that is analogous to what is observed when a patient whose tissues are saturated with nitrogenous refuse begins a course of diet from which flesh is eliminated. The toxic compounds that had been stored in the tissues where their noxious action was minimized to the lowest degree now become soluble and are transported by the circulating fluids to the nervous tissues, where they produce feelings of depression, despondency, and exhaustion that will persist until the whole surplus has been discharged from the body. Sudden changes alike in diet and exercise are therefore to be deprecated, and in all things the system must be gradually habituated to the new order of life.

Bathing.

Baths of all kinds may be employed with considerable advantage, if rightly used. But it must be always kept in mind that arthritic subjects are far more sensitive than others to heat and cold, and to variations of temperature. For this reason, if for no other, such persons must exercise more than ordinary caution in the matter of bathing. Since the act of taking a bath is in many respects equivalent to active exercise, the same rule that applies to muscular exertion should control the use of baths. Moderation is the rule. The patient must not indulge too frequently nor for too long a time. The age and vigor of the subject should also be taken into consideration. For young and vigorous people, whose viscera are still in a healthy condition, cold plunge-baths may be permitted. If the patient be of a delicate organization, cool sponge-baths, followed by vigorous friction with coarse towels and brushes, should have the preference. But if there be feeble reaction after the bath; if there be an abiding sense of chilliness, with a cyanotic hue upon the skin, cold bathing must be forbidden, especially if there be any suspicion of renal insufficiency. In all such cases, warm baths are indicated. The particular kind of warm bath must be ordered after careful examination of the individual peculiarities of the subject. Warm-water baths are to be recommended for those who can remain indoors during the greater part of the time, and for the victims of renal or hepatic or nervous disorder. The bath should be of short duration, and should be followed by repose in bed for an hour before exposure to cold air. Such a bath may be taken in the morning before breakfast, and be followed with a cup of hot milk colored with tea or coffee; then, returning to bed, the patient will easily sleep till noon, when he should dress, and partake of a temperate breakfast according to the diet-list recommended on a previous page. For patients who are full-blooded

or who are suffering with obesity, considerable caution is necessary, for they are often greatly debilitated by long immersion in hot water, and by the copious perspiration that follows. Such persons should take dry hot-air baths, if heat be desirable, since they are more stimulating than vapor baths or warm-water baths. Many patients who experience a sensation of suffocation in a Russian steam bath can sit in the hot room of a Turkish bath with perfect comfort. Whenever there is a tendency to bronchial catarrh, or when the heart is enfeebled by any cause, dry hot air is much more tolerable than moist heat. In the majority of cases that can tolerate these baths, the ultimate effects are beneficial. At first, there may be complaint of exhaustion and depression of spirits, for the reason that perspiration increases the alkalinity of the blood and its power of holding urates and other nitrogenous substances in solution. Thus dissolved they are conveyed to the nervous centres, where such substances as paraxanthin, gerontin, etc., exert their toxic influence, which is manifested under the form of exhaustion, debility, and extreme mental depression. After a time, however, especially if the diet be properly regulated, and the hepatic excretions be aided, these substances are so far eliminated as to produce a complete change in the condition and feelings of the patient. The first experiences of one who undertakes a course of such baths cannot, therefore, determine the final result.

Sea-bathing is usually the equivalent of a cold bath. It is only permissible to those who are young and comparatively healthy. Through the constringent effect of cold, the perspiration is checked and the blood becomes less tolerant as a medium for the solution of nitrogenized substances. Urates and their congeners are, however, not diminished in the urine unless the patient is kept on a rigid diet. When people visit the seaside their baths and exercise usually cause an increase of appetite which they gratify without stint, unless kept under medical supervision; hence occurs a considerable increase of urea and the other nitrogen compounds in the urine. An intelligent oversight is therefore necessary in order to keep the balance even between the elimination that is due to baths, exercise, and bracing air, and the nitrogenous intake that is increased by an improving appetite. Still, it will be ordinarily found that, like all other forms of activity in the open air, the influence of sea-bathing is very wholesome. It is excessive indulgence and exposure to chill, with consequent disorder of the liver and kidneys, that are to be avoided in every case. Hydropathic treatment is unattended by many of the dangers that accompany the ordinary use of baths. For young and vigorous subjects it is an admirable expedient; but for the old and feeble it must

be employed with great caution. The use of cold douches and other similar methods of applying cold water must be guarded by the same precautions that are necessary with regard to cold baths. It is wise to form in youth the habit of cold sponging of the surface, for then the practice can be continued through life with great advantage to the patient; but to begin the use of the sponge bath at an advanced age, after the constitution has been undermined by disease, is not without considerable danger. Still, when the heart and kidneys are yet intact, great benefit is sometimes obtained from cold affusions followed by vigorous friction and massage. Horace has recorded his indebtedness to these methods (Epist., Lib. I., 15):

"Mihi Baias
Musa supervacuas Antonius, et tamen illis
Me facit invisum, gelida cum perluor unda
Per medium frigus."

And it was by similar advice to the Emperor Augustus that Antonius Musa acquired his great reputation in ancient Rome. Especially valuable is this practice during hot weather, when the patient is debilitated by heat and excessive perspiration. If possible the treatment should be commenced under medical advice in a well-appointed hydropathic establishment, and then its good features can be perpetuated subsequently at home. But for elderly people, it is generally necessary to avoid all sudden chilling of the body; dry friction and massage, either with or without the application of aromatic and stimulating liniments, are decidedly preferable. In this way the healthy function of the skin can be most efficiently secured. The inordinate sensitiveness of gouty people renders it also necessary for them to guard against the impressions of atmospheric change. They must wear flannel underclothing throughout the year, shifting from heavier to lighter stuffs during the summer, but never abandoning woollens altogether. Such patients perspire abundantly upon the slightest provocation, and frequently they experience night-sweats that remind one of the damps of tuberculosis. For this reason, it is often expedient to wear thin woollen night-gowns instead of the ordinary cotton garments. During the colder half of the year elderly subjects derive great comfort from flannel sheets on their beds at night, particularly if there be a tendency to perspiration or to coldness of the feet and legs. Whenever their circumstances will permit them to enjoy the luxury of travel, they should become birds of passage, seeking to pass the months of autumn, winter, and spring in countries where the air is dry and warm. For this purpose, the interior regions of Algiers, Tunis, Arabia, India, and Ceylon, the West India Islands, Southern California, certain portions of Mexico and Central America,

and the Hawaiian Islands can be confidently recommended. If such liberty of choice cannot be afforded, it may still be possible to find a home at a distance from the ocean, or any other large body of water. Even a cold climate is preferable, if it be dry, to the chill and damp that prevail along the sea-coast. In this respect the air of mid-ocean is far more tolerable than the fogs and rains that veil the northern shores. For those who are fond of sailing, a long voyage is often beneficial, especially if it be taken in an old-fashioned sailing-ship, slowly gliding through the trade-wind belt, where for weeks together the temperature of the air and the stainless blue of the sky remain unchanged. There, remote from the toil and turmoil of civilization, can be found such rest as no other spot on earth affords. And if at the end of the passage lies the Cape of Good Hope, or Australia, or Northern New Zealand, or the Isles of the Blest, he must be indeed an arthritic veteran of the most obdurate sort who does not experience a renewal of youth and health under these favorable conditions.

Medicinal Treatment.

Having thus passed in review the principal hygienic measures that are efficient in the preventive treatment of the arthritic diathesis, we may proceed to the consideration of certain therapeutical agents that have acquired a reputation in the same field.

Basing their practice upon the fact that in the presence of ozone uric acid is transformed into urea and other more completely oxidized compounds, a number of theorists have proposed to treat gout by inhalations of oxygen, and have reported favorable results. But it is probable that whatever good effect accrues from such experiments is due to the increase of muscular effort and consequent improvement of the circulation for a short time after the inhalation. Any one who suffers with arthritic neuralgia of the abdominal viscera will notice a similar temporary alleviation of pain after a number of deep and rapid inspirations of ordinary air. These exercises give help in about the same way that muscular exercise benefits functional nervous disorders of the heart that are caused by dyspeptic toxæmia. As a practical fact, however, it will be seldom possible to persuade any considerable number of patients to breathe out of a bag or a cylinder for a long period of consecutive days. Mountain-climbing and an out-door life will be found far more efficacious and agreeable.

Alkalies.

From the remotest antiquity the alkaline salts and their bases have enjoyed the highest reputation in the treatment of gout. Long before

the birth of chemistry the ancient Greek physicians in Alexandria, Athens, and Rome were in the habit of giving to their arthritic patients a weak lye prepared from vegetable ashes. These ashes contained a notable quantity of the carbonates of potassium and sodium. The German physicians during the Middle Ages, and later, prepared a similar decoction of ashes diluted with Rhine wine. Nitre also had its advocates. Cullen and his followers noted the fact that all of the mineral alkalies were effectual to postpone the attacks of gout, and to prevent the appearance of urates in the urine. The great advances of practical chemistry have placed before the modern physician a large number of alkaline salts, of which all are useful, though many of them differ in their immediate effects.

The action of these various alkalies does not simply consist in their power of neutralizing acids. While it is true that the carbonates and bicarbonates do serve to antagonize over-acid conditions of the stomach and duodenum, and to cause the disappearance of acidity from the urine, it is highly probable that they stimulate the secretion of the gastro-intestinal glands, together with the pancreas and the liver. Claude Bernard's often-repeated experiment upon the mucous membrane of the stomach of a dog illustrates the great increase of secretion that follows the introduction of a little Vichy water into the stomach. A similar effect of alkaline waters upon the discharge of bile through a canula introduced into the common bile duct has been repeatedly observed. The administration of alkalies must, therefore, be followed by an increase in the amount and activity of the digestive fluids, and by improvement in the functions of absorption, assimilation, and excretion. Under such circumstances the general nutrition cannot fail to be improved. Accordingly, after a prolonged course of medication the highly acid urine that is characteristic of the arthritic diathesis becomes neutral or only feebly acid; and it often remains in this condition for a considerable time after the treatment has been discontinued.

The action of alkalies in the blood is still very imperfectly understood. As a result of his laboratory experiments Sir William Roberts declares that the addition of alkaline salts to a solvent medium at the temperature of the blood does not materially affect the solubility of sodium bi-urates. He says (*loc. cit.*, p. 82): "The influence of a salt depends exclusively on the nature of the base, and has no reference to the acidulous radicle with which the base is combined. Salts with an alkaline reaction, such as carbonates and phosphates, do not differ in the least from neutral-reacting salts, such as chlorides and sulphates. The salts of sodium exercise a strong deterrent influence (upon solution), and the deterrent influence increases with the

increasing percentage of the salts in solution. Salts of calcium, magnesium, and ammonium have also a deterrent effect but slighter than that of salts of sodium. Salts of potassium have no effect either way."

These laboratory experiments, however, are of slight value in comparison with the results of observation at the bedside. Haig and many others have shown that the ingestion of alkalies causes an increased discharge of urates with the urine. As he can find no evidence that the ratio of formation between urea and uric acid is ever disturbed, it follows that the increase of urinary urates is due to the greater capacity of the blood for soluble urates, which by the aid of alkalies are washed out of the tissues where they had been previously deposited. How this process is effected is not yet explained, for the experiments of Sir William Roberts have made it clear that the mere addition of alkaline salts to a solvent medium does not increase its power to dissolve the bi-urate of sodium—the combination in which uric acid exists in the body. Doubtless, the chemical processes by virtue of which the bi-urates are transformed into quadri-urates, and the solidified salts are again rendered soluble, and *vice versa*, are far more complicated than anything that we have yet seen in the test-tubes of the chemist. It has been suggested that di-sodium phosphate (Na_2HPO_4) is the agent that acts as a solvent of uric acid in the blood, and that its efficiency is maintained by the presence of alkalies which prevent its degradation to the acid sodium phosphate (NaH_2PO_4), a substance that is powerless as a uric-acid solvent. Could this inference from laboratory experiment be verified upon the living subject, it would be a great gain to science. The relation of all these alkaline substances to excretion, especially with reference to the elimination of the poisonous compounds of the xanthin group, needs additional investigation.

Considerable difference of opinion has existed with regard to the general effect of treatment with alkalies. Some of the most distinguished teachers have condemned the extended use of such salts, claiming that they destroy the red corpuscles of the blood, and produce a most debilitating effect upon the system. On the other side, Charcot and his pupils declare that such results are of the rarest occurrence. They have for months together given to their patients as much as an ounce a day of sodium bicarbonate, without the slightest ill-effect. There is, however, considerable difference among people with regard to the tolerance of such compounds, so that it is always necessary to study the idiosyncrasies of the patient before advancing to the use of such large doses. In the treatment of gout the same rule holds good that is to be observed in the medication of syphilis with mercury—do not administer the alkaline salts

in massive quantities when there are old age, anæmia, and atonic conditions complicating the case. To the young and vigorous patient these remedies may be safely given to the extent of three or four drachms a day; but under other circumstances they must be wholly withdrawn, or used only in small quantities.

The various alkaline salts cannot be used indiscriminately in place of each other. The compounds of potassium are much more energetic than those of sodium, and are therefore less easily tolerated by the organism. They do not, according to Sir William Roberts, exert any directly solvent influence upon uric acid, but they are more powerfully diuretic than the corresponding sodium salts, consequently they aid the process of elimination through the kidneys. The potassium salts enter into combination with the red blood corpuscles, and with the protoplasm of the connective-tissue and muscular elements. They modify the processes of nutrition in those parts, and may even act as a poison to muscular substance, while the salts of sodium are chiefly found in the plasma of the circulating fluids by which they are readily tolerated.

An interesting fact regarding the salts of lithium has been brought to light by Haig (*loc. cit.*, p. 30). Owing to the easy solubility of uric acid in solutions of lithia and its salts, it has been everywhere taken for granted that lithia waters must be very useful as agents for the removal of uric acid from the system. Great ingenuity has been accordingly displayed in the exploitation of mineral springs that were supposed to yield the precious mineral. But Haig, in the course of his experiments, discovered that "lithia diminished the excretion of uric acid." The cause of the paradoxical fact is set forth in Rose's "Chemical Analysis" (p. 15), where it is stated that lithia taken internally is of no use as a solvent of uric acid, because it "forms a nearly insoluble triple phosphate with phosphate of soda, or with the triple phosphates of ammonia and soda, salts generally present in animal fluids." Whatever value may therefore attach to lithium salts is due to their simple diuretic action, and to the manner in which they drive urates out of the blood into the tissues, rather than to any superior solvent power such as they exhibit in the test-tube of a laboratory chemist.

The salts of magnesium are useful evacuants in acute gout, but are inferior to the potassium compounds in the treatment of the patient during the intervals between the attacks, or during the stage of chronic gout. Especially useful are the potassium salts in subacute cases when urates begin to accumulate in and about the joints. They should then be administered in doses of thirty to fifty grains a day of potassium carbonate, for a long period of time. Under simi-

lar circumstances the phosphate of ammonium may be employed with considerable advantage. It is actively diuretic, and has the advantage of being non-toxic to the tissues. Sir Dyce Duckworth recommends its use in cases of gouty glycosuria in doses varying from ten to forty grains a day. It may be used in larger quantities with safety, even as high as five or six drachms per diem. Sodium phosphate, if chemically pure, is a useful diuretic solvent of the urates, and in large doses is pleasantly aperient. It may be given in doses of one to four drachms two or three times a day, according to its effect upon the bowels. Its comparative tastelessness and its harmless action render it a valuable salt for those who need a laxative that can be tolerated for very long periods of time. It is especially useful in torpid engorgement of the liver, and may be advantageously taken in a hot solution every morning before breakfast.

As a general rule it may be asserted that the salts of sodium are safer and better tolerated than the other alkaline salts. It is, however, sometimes advantageous to employ the different basic compounds in association, somewhat after the manner of their occurrence in the natural mineral waters. Thus Dr. Alfred Hinde, of Chicago, has made extensive use of the following formula, with most happy results in cases of headache, indigestion, constipation, neuralgia, asthmatic bronchitis, etc., dependent upon the arthritic diathesis:

℞ Tr. quassiæ,
Tr. calumbæ,
Spt. chloroformi,
Spt. vini rect. ..... āā ʒ ss.
Sod. bicarb. solut. saturat. ..... ʒ ij.
Sod. sulph. solut. saturat.,
Magnes. sulph. solut. saturat. ..... āā ʒ vi.
M. Filter. Sig. Take a tablespoonful in a glass of water, half an hour before each meal.

Iodide of potassium is of little value during the acute stage of gout, but in the chronic form of the disease, administered for a long time with tonic doses of quinine, it is of great utility.

Salicylic and Benzoic Acids.

Sodium salicylate is the form in which salicylic acid is usually exhibited. Too great care cannot be taken to procure a pure specimen of the drug. Many of the failures in its use are the result of impurities in the medicine, as well as of timidity in its administration. Inexperienced physicians who give small doses of an impure preparation have very little idea of the remedial effects that can be obtained

from the employment in sufficient quantity of an unadulterated article. It is in the acute stage of gout that its action is most conspicuous, when given in doses of fifteen to twenty grains every two hours. In hemicrania, in trigeminal neuralgia, gastro-enteric pain, and other forms of neuralgia that are dependent upon the gouty diathesis, it is one of the most efficient agents for the relief of suffering. It is most effectual when administered in connection with the mineral acids. Thus in hemicrania the patient should take fifteen to twenty drops of dilute nitro-hydrochloric acid after each meal, and ten grains of sodium salicylate before meals. In tic douloureux the sodium salt may be administered every two or three hours, with great advantage in plethoric cases. But in atonic and chronic cases colchicum and other hepatic evacuants will probably be needed in addition to the alkaline salt. Haig has also called attention to the fact that it is only in typical cases of gout and rheumatism that the salicylates are beneficial. In gonorrhœal and traumatic affections of the joints they are useless, apparently because in such cases there is no surplus of urates to be evacuated.

The well-known action of benzoic acid, by which it enters into various combinations within the tissues, and is finally eliminated as soluble hippuric acid in the urine, has led to its therapeutical exhibition in arthritic conditions. Contained in vegetable food it is the active agent by reason of which the graminiverous mammalia always excrete hippuric acid instead of uric acid. The alkaline hippurates are very soluble, while the urates are quite the contrary. Upon the basis of these observations, benzoic acid and its sodium and ammonium salts have been employed with considerable success as eliminants of uric acid. These preparations may be given in doses of ten to twenty grains every three or four hours. They are easily tolerated by the alimentary canal and by the urinary passages. They are especially useful in catarrhal conditions of the bladder, and when there exists a tendency to offensive decomposition of the urine in the vesical cavity. Hence their utility in cases of senile gout, in which such complications are not infrequent.

Mineral Acids.

The action of the mineral acids, in disordered conditions dependent upon the arthritic diathesis, is quite as pronounced as that of the alkaline salts. They often give great relief to many nervous symptoms that arise under such circumstances, but their mode of action is the reverse of that which is characteristic of the alkalies. They tend to increase the acidity of the blood, and thus to drive the nitrogenous excreta into the tissues where the poisonous effects of the

xanthin compounds are less conspicuous. In this way great temporary relief from nervous symptoms may be procured. But unless curative measures in the way of proper arrangement of the diet and habits of life are also employed, the period of relief will be followed by an increased severity of the original symptoms when the supersaturated tissues again discharge their morbid contents into the current of the circulation. The best results of the employment of mineral acids are apparent in the example above given of their utility in the treatment of hemicrania. Administered alone, they clear the blood of nitrogenous toxins, but do not sufficiently eliminate them from the body. This is accomplished by the concurrent exhibition of sodium salicylate, which eliminates, and also exercises a directly anodyne influence upon the sensory apparatus. In catarrhal states of the gastro-enteric mucous membrane the mineral acids are equally beneficial. By their remedial influence upon the catarrhal inflammation, they diminish the over-acidity of the blood that depends upon the adjacent inflammation, and thus they favor the elimination of nitrogenous refuse through the increased capacity of the circulating fluids for the solution and transportation of such excreta to their place of final elimination in the kidneys. While this process is going on, the administration of ten- or fifteen-grain doses of sodium salicylate every four hours will often give the greatest relief in those cases of gastralgia and enteralgia that so frequently torment the arthritically predisposed subject. The action of acids upon the liver is also of the greatest importance in this connection. The eliminative effect of nitro-hydrochloric acid is well known, and it is in this way that much of its beneficial action is produced.

Purgatives.

The employment of purgatives in the treatment of gouty conditions must be conducted with moderation and precaution. Cholagogues and cathartics are for the most part beneficial only so far as they promote good digestion and obviate hepatic congestion. For this reason it is unwise to have recourse to violent purgation as a means of clearing the system of toxic substances. Gentle and stimulating laxatives are preferable to any powerful cathartic drug. Rhubarb, aloes or aloin, euonymin, podophyllin in small doses, guaiacum, sulphur, and magnesia are the favorite laxatives. In many instances, where the liver is engorged, and the hemorrhoidal veins are over-distended, a few doses of calomel or blue-pill are very beneficial. The following prescription is often of great value in such cases:

℞ Pil. hydrarg. mass.,
Ext. colocynth. comp.,
Ext. colchici acet.,
Ext. hyoscyami.....āā gr. vi.
M. Div. in pil. No. vi. Sig. Take one pill every four hours till the bowels are sufficiently moved.

The old-fashioned "black draught" also renders excellent service in many of these cases.

When acid dyspepsia is troublesome, much relief may be obtained from the various preparations of magnesia, or from the bicarbonate of sodium. The ordinary neutralizing cordial and the mistura rhei et sodæ are valuable laxatives in such cases. In mild forms of gastro-intestinal catarrh, with constipation and a tendency to dull headaches, great benefit may often accrue from the protracted use of sulphur and bitartrate of potassium, in small doses combined in a soluble tablet. One or two such tablets after each meal will be found very useful in obstinate cases of constipation.

Podophyllin, colocynth, colchicum, and all of the more energetic cholagogue cathartics should be used in small and laxative doses. It was probably a neglect of this precaution that led Sydenham to condemn the use of cathartics in gouty conditions of the body. There can be no doubt that their abuse tends to the production of debility, and to the degradation of acute forms of gout into the chronic and atonic varieties of the disease. Whenever it is desirable to obtain a laxative effect together with gentle stimulation of the cutaneous circulation, guaiacum will be found beneficial. It may be given in doses of five grains with a scruple of potassium bicarbonate in half a tumbler of lemonade. This forms a pleasant effervescent draught that disguises the taste of the powder in a very satisfactory manner. Repeated every four hours this prescription is very effectual in gouty tonsillitis, and in cases of myalgia and "muscular rheumatism" which are so often of gouty origin.

Mineral Waters.

The employment of mineral waters in the treatment of arthritic states of the body is very extensively practised. But it is often difficult to estimate the exact value of this method because so many elements enter into the result. When the weary man of letters and the tired official find rest and freedom from care in a pleasant mountain retreat far from the maelstrom of modern civilization, great credit must be given to the change of scene and to the relief from routine and intellectual fatigue. When the over-fed denizen of the damp and gloomy sea-coast inhales the pure, dry air of the continental interior,

much of the benefit that he experiences must be ascribed to this wholesome transformation of his environment. After all these factors have been taken into account there remains, however, a certain residuum of advantage that must fairly be attributed to the effect of certain mineral waters that have been pronounced, after long experience, to be particularly remedial in the treatment of arthritic conditions.

During the crises of acute gout the use of mineral waters is ineffectual—it may be actually injurious. Large draughts of ordinary water are hurtful in acute indigestion; and disorder of the stomach is one of the most prominent symptoms in these crises. If mineral waters of any kind are to be prescribed during this stage of the disease, they should belong to the alkaline group, of which the Vichy waters form the type. These contain about one drachm of sodium bicarbonate to the quart, and are to be drank while warm at their natural temperature. But for the vigorous, though chronic, sufferer from subacute forms of arthritism, for the great eater and drinker with hepatic engorgement, catarrhal gastro-duodenitis, dyspepsia, somnolence, and general plethora, the stronger waters of the Karlsbad type are to be preferred. These contain sodium sulphate, and are quite laxative, hence their beneficial effects upon the congestive states and catarrhal conditions by which these patients are disabled. When there exists a tendency to diabetes or to gravel, waters that contain very little mineral matter are most useful. Of these the waters of Contrexéville in France, of the Poland spring in Maine, and of Waukesha in Wisconsin, are typical. When the joints have become stiffened by repeated inflammation and earthy deposits, hot baths are most useful. Of these the numerous hot springs in different parts of the world are all efficacious when there exist no cardiac nor pulmonary complications to contra-indicate their use. But, since the application of moist heat is the principal agent in this mode of treatment, nearly equal effects can be obtained from daily tub-baths, accompanied by active massage at home. When the cutaneous surfaces are affected by chronic eruptions of arthritic origin, hot sulphur baths are to be recommended. Chalybeate springs are seldom of service in gout. Iron is one of the agents that cause accumulation of urates in the tissues, hence its action is favorable only after a long course of eliminative treatment.

Having thus briefly outlined the general rules for the employment of mineral waters it will be useful to consider at greater length the special indications for their exhibition. It is well known that pure table water is diuretic and to a certain extent laxative. In cases that are characterized by the formation of gravel and by the accumulation of uric-acid sand in the pelvis of the kidney, great benefit is often de-

rived from a sort of "flushing process" with potable waters that contain very little mineral matter. Of this description are the waters of Wildbad in Germany, Contrexéville, Evian, and Vittel in France, Bath in England, and the Poland and Waukesha springs in the United States. These waters are especially valuable in cases of obesity, arthritic diabetes, and dyspepsia with sluggish kidneys and scanty, highly acid urine. They stimulate all the excretory functions, and are easily tolerated by the mucous membranes of the alimentary canal. After a course of Poland spring water, an astonishing quantity of uric-acid sand is sometimes evacuated, with great and persistent relief from the lumbar pain that had previously harassed the patient.

For young and vigorous subjects the thermo-alkaline waters are to be preferred. Of these the world-old Vichy water is the typical example. Waters of this class are powerfully alkaline, being charged with sodium bicarbonate and carbonic acid gas. They contain very little chlorine, and the salts of potassium, magnesium, and calcium are present in comparatively small quantity. Under their influence all the functions of the body are stimulated, and the urine losing its acidity is copiously voided. It is said that while one is drinking these waters an acute attack of gout may be induced through their influence. Probably, however, this is largely due to the fact that the Vichy Springs are visited by numerous patients who have postponed medication until it is too late to avert a threatened crisis. But it is certain that these waters cannot be taken in large draughts. By reason of their elevated temperature and composition, they must be taken in moderation, especially at the beginning of a treatment. It is believed by those who are experienced in their use that without such precautions articular symptoms may be diverted to the internal viscera. As a general rule, it is therefore advisable to administer the waters during the intervals between the attacks of gout. Thus employed the crises may be rendered less severe and less frequent—the gastro-enteric catarrh that exists in the majority of arthritic subjects is cured, and the general health is thus greatly improved.. Such complications as obesity, arthritic diabetes, and lithiasis are wonderfully relieved by the use of the waters. Sometimes, after a course of treatment at Vichy it is advantageous to take a supplementary course at Vals, where the water contains chlorides in association with sodium bicarbonate. The waters of Royat, containing iron and arsenic, as well as alkaline saline constituents, are especially useful in the cutaneous disorders and mucous inflammations of the pulmonary and gastro-intestinal tracts. The springs at Néris and La Malou are to be preferred for feeble and nervous invalids who cannot tolerate the

stronger waters. In Germany the springs at Ems and Fachingen are to be recommended for similar mucous affections. In the United States there are few purely alkaline waters, and they do not begin to equal the strength of the Vichy waters. The Bladon springs in Alabama; the Congress and the Seltzer springs in California; the St. Louis spring in Michigan; and the Sheldon springs in Vermont, are among the best-known sources of the class.

For patients of a plethoric habit who suffer with hepatic congestion and constipation, waters of a laxative character are desirable. These are furnished by springs which contain sodium chloride and sodium and magnesium sulphate. Karlsbad affords the type of this class of waters. By reason of their laxative character they are less likely than the Vichy water to produce visceral congestion. They should not be drank during the crises of acute gout; and they are not adapted to the wants of the anæmic and asthenic victims of chronic arthritism. But for recent cases of a plethoric character they may be prescribed during the intervals with great advantage. The waters of Kissingen, Marienbad, Homburg, Püllna, Friedrichshall, Racoczy, Wiesbaden, and Baden-Baden represent this class in central Europe. The Rubinat water from Spain is an excellent purgative. In France, the waters of Châtel-Guyon are highly recommended for the more vigorous patients, while for those who are debilitated the springs of Saint-Nectaire and of Brides are preferable. In America the Canadian springs at St. Catherine's and at Caledonia, the wells at St. Clair, at Mount Clemens, and other places in Michigan, the Saratoga springs in New York, and the Crab Orchard springs in Kentucky, are among the most valuable representatives of the saline group. In Great Britain the waters of Harrowgate, Leamington, Cheltenham, and Llandrindod are similarly useful. The mineral waters above mentioned produce very little effect upon old uratic concretions about the joints.

For chronic forms of gout with articular deformity thermal waters are most useful. These vary considerably in the composition of their mineral ingredients. Some of them, like the waters of Teplitz, Plombières, Buxton, Bath, and the Arkansas Hot Springs, contain very little earthy or saline matter; while the Wiesbaden springs, the Glenwood springs in Colorado, and the Hot Springs in South Dakota are rich in chlorides and other salts. The thermal waters of Plombières, Bourbonne, Balaruc, and Bourbon-l'Archambault in France are highly esteemed for their resolvent power. Many of the thermal springs contain sulphuretted hydrogen, and this adds to their value when employed in the form of hot baths. The patient should be subjected to massage while in the bath, and the affected

joints should be gently rubbed and flexed, to promote resolution of the uratic deposits. But this active form of treatment is always contra-indicated in cases of cardiac or arterial or intracranial disease.

The mineral springs within the area of the United States are very numerous, and some of them possess considerable value in the treatment of gout and the allied affections. A convenient classification of their characteristics and territorial location is furnished by Beaumont Small ("Reference Handbook of the Medical Sciences," Vol. IV., p. 694). According to this author, the waters that are "found in the western mountainous district, which extends from the Pacific coast almost to the Mississippi River, are chiefly alkaline springs containing a few grains of the purgative salines, generally of a high temperature and strongly sulphurated. Thermal salines, with and without sulphuretted hydrogen, also occur, such as the Utah and Calistoga springs. In the East the highly carbonated and alkaline-saline springs are the most common. The only thermal springs are in Virginia and the South. These are only slightly sulphurated and almost imperceptibly alkaline. In the great paleozoic basin, which formed the bed of the early sea, we naturally find the waters rich in salines. Those containing chlorides are to be found everywhere, but such as contain the purgative sulphates are chiefly confined to certain districts, as in Kentucky, Michigan, and western New York. In these the active salt is sulphate of magnesium. In this they differ from the purgative waters of the West, which owe their properties to sulphate of soda." In Canada the springs are "chiefly saline and alkaline-saline; a large proportion are ferrated and sulphurated."

Treatment of Acute Gout.

Having thus passed in review the most important of the elements in the treatment of gout—important because they relate to the daily life and habits of the arthritic subject—it remains to consider the measures that are necessary in the management of the acute crises which constitute the most conspicuous feature of the arthritic diathesis. Opinions regarding the treatment of the attacks have greatly varied during the course of time. Celsus and Galen advised copious blood-letting, while Sydenham and Cullen advocated an expectant method. Some have regarded acute gout as a disease to be combated and suppressed by abortive treatment: others regard it as a beneficial crisis that should be permitted to run its own course. Modern practice inclines toward the adoption of a medium course that shall aid and support the body during the critical evacuations

that constitute the attack, and that shall serve to mitigate the sufferings of the patient so far as that can be accomplished without interfering with the natural course of events.

In a majority of cases the symptoms are not marked by a degree of intensity sufficient to require active intervention on the part of the physician. The patient should be kept in bed during the attack and the diet should be restricted so long as a febrile movement exists. Copious draughts of pure water should be encouraged in order to quench thirst and to promote the action of the skin and kidneys. Our forefathers under such circumstances were great admirers of herb-tea. In modern times such inert beverages as Poland water, Buffalo lithia water, and the simple aerated waters have acquired for themselves the reputation that was formerly connected with barley water and other harmless infusions. The various granular effervescent salts of lithium, potassium, and sodium may be also given with good result in the way of increasing the flow of urine and thus aiding the natural eliminative processes. Active purgation is unnecessary in these cases. In the course of a week the tongue cleans, the appetite returns, pain subsides, and convalescence begins without the employment of active measures.

But, when the crisis is violent and painful, it becomes needful to moderate its severity. If the heart and kidneys are yet intact, considerable latitude is permissible in the exhibition of remedies. If, however, these important organs are materially injured by disease—if the pulse be weak and irregular, and if there be albumin in the urine great caution is necessary, and the treatment should be principally devoted to the application of local remedies to the affected joints. When the patient is young and vigorous, he should be kept in the recumbent position, with the inflamed joint upon a well-adjusted cushion by which the limb can be supported a little above the level of the body. The application of leeches is no longer practised, since it has been shown to be either without effect or positively injurious. But much relief from pain can often be procured by the use of hot fomentations—hot whiskey and water applied on flannels covered with thin rubber cloth or oiled silk. In the same way may be applied the time-honored lotion of lead water and tincture of opium. Sir Dyce Duckworth praises the following combinations:

℞ Lin. belladonnæ ..... f ℥ iij.
Morphinæ hydrochlorat. ..... gr. x.
M. et ft. liniment. Sig. A teaspoonful to be mixed with a tablespoonful of hot water and applied on lint under oiled silk every four hours.

℞ Atropinæ ..... gr. iij.
Morphinæ hydrochlorat. ..... gr. xv.
Acidi oleici ..... f ʒ i.
Solve et ft. liniment. Sig. To be painted over the painful joint with a large camel's-hair brush, and carded cotton to be superimposed and retained with a bandage.

Three parts of menthol and two of camphor may be rubbed up together to form an anodyne application, or ℥ ss. of menthol may be dissolved in f ℥ vi. of spirit of chloroform for a lotion.

Four grains of cocaine may be dissolved at a gentle heat in ℥ ss. of oil of sweet almonds, or of oleic acid, to form an anodyne liniment. Internal medication in this class of patients should begin with the administration of a mercurial cathartic—either a few grains of calomel followed by a glass of effervescent citrate of magnesia, or

℞ Pil. hydrarg. mass.,
Ext. colocynth. comp.,
Ext. colchici acet.,
Ext. hyoscyami ..... āā gr. vi.
M. Div. in pil. No. vi. Sig. Take one pill every three hours until the bowels are moved.

For the relief of pain, the local use of anodynes, as above described, is usually sufficient. Hypodermic injections of morphine have been made occasionally in the vicinity of a painful joint, but the practice is attended with some danger of metastasis, followed by the development of the symptoms of retrocedent gout. There can be, however, no objection to the moderate use of small doses of morphine —the thirtieth of a grain every hour for example. These minute and frequently repeated doses relieve nausea, allay irritation, promote perspiration, and exert an appreciably anodyne effect. When considerable fever is manifested, a drop of the tincture of aconite may be also given with each portion of the morphine. But such medication is only adapted to cases of moderate severity; it would avail but little in the stormy crises that sometimes occur.

A few years ago, when anti-thermal medication was in vogue, large doses of sulphate of quinine were often used as a febrifuge during the feverish stage of the attack. This mode of treatment has now become almost obsolete, and has been superseded in the majority of cases by the exhibition of sodium salicylate. The conditions of success in the employment of this drug are dependent upon the chemical purity of the remedy and the efficiency of its administration. The impure salt is often very irritating to the stomach, and may produce cerebral symptoms that are indistinguishable from those of delirium tremens. If given in insufficient doses no appreciable result

is apparent, and the remedy is accordingly discredited. But when employed as it is in acute rheumatism, in doses of ten grains every two hours, great relief is soon experienced. Under its influence pain and fever are reduced, perspiration increases, and the flow of urine becomes profuse. The discharge of urates is augmented, and the tissues are relieved of this cause of irritation. When this result has been attained, the frequency of administration may be reduced, but it is well to continue the remedy for ten days or two weeks, in doses of ten grains, three or four times a day. When the stomach is intolerant of the powdered salicylate or its solution, it will often endure the medicine in the form of tablets which dissolve slowly and present the drug more gradually to the mucous membrane. In advanced cases of gout, with diseased heart and kidneys, the drug cannot be given as liberally as in the case of a young and vigorous subject.

The remedy that most nearly approaches the rank of a specific for gout is colchicum. This substance is a drastic purgative that acts powerfully upon the nervous system, and tends to produce a state of collapse like that of cholera, if given in considerable doses. In all this there is nothing to suggest its special qualities for the relief of gout. Known to the ancients, it has maintained its reputation for thousands of years. Its effects are most conspicuously manifested in the joints that are the seat of acute inflammation. Under its influence pain and swelling rapidly subside, and in a few hours the affected part resumes its ordinary appearance. The English physicians advise delay in the exhibition of the remedy until the local symptoms are fully manifest in the joint that is the seat of the attack. Then the drug should be given, in the form of either the wine or tincture of the root or of the seeds. The tincture of the seeds is stronger than that of the root, and is the preparation usually employed by American physicians, though the wine of the seeds is with many a favorite preparation. The remedy should be given in diminishing doses—from 30 to 45 minims at night, and half that quantity in the morning. As the severity of the symptoms is reduced, these doses may be correspondingly lowered, but it is well to give small doses of the medicine for weeks and months together during periods of protracted and imperfect convalescence. Sir Dyce Duckworth praises the *Haustus colchici* of St. Bartholomew's Hospital Pharmacopœia:

℞ Magnesii carbonat ..... gr. x.
Tinct. sem. colchici ..... ♏ xx.
Aq. menth. virid ..... ad f ʒ i.

This may be given night and morning as required.

The beneficial effect of colchicum is not due to its purgative energy,

and Sir A. Garrod has shown that it does not augment the discharge of urea or the urates. Rutherford has shown that the drug is a most potent cholagogue—probably one of the most energetic in existence. By its action upon the liver it accomplishes an amount of elimination that can be produced in no other way. It probably also exerts a specific influence upon the nervous system by which the processes of inflammation are corrected. For these reasons colchicum, in some form, may be found in the majority of the quack nostrums that are so commonly employed by the public. But in this unquestionable energy lies the danger that accrues from its indiscriminate use. It is advisable to avoid all drastic purgation, hence it is well in cases that present any appearance of debility to begin the treatment with moderate doses. In certain cases there is an unusual susceptibility to the poisonous effects of the drug, and it is not impossible that some of the examples of so-called retrocedent gout with choleriform symptoms have been really instances of colchicum poisoning. The active principle of the plant, colchicine, has been sometimes employed as a substitute for the ordinary officinal preparations; but the intense energy of this substance renders its extensive use quite inexpedient. The same thing may be said of veratrine—it is exceedingly poisonous, very unreliable, and rarely beneficial.

Against the use of colchicum has been urged the objection that its employment tends to transform acute gout into the chronic variety of the disease. But this is the natural tendency of the malady. As years progress, and the body becomes enfeebled with age, the attacks of articular inflammation become less violent and are more protracted in their duration. Sir A. Garrod has shown that in many instances this degradation of the symptoms is reached at a comparatively early period without medication of any kind. On the other hand, there are patients who all their lives have taken colchicum, in the form of quack remedies or at the hands of intelligent physicians, and yet have never experienced anything but acute crises of gout such as they first knew in early life. It is now generally admitted that, properly used, colchicum is a perfectly harmless remedy. It certainly has never been superseded by any other drug.

Recently a preparation by the name of piperazine has been widely advertised as a solvent of uric acid. It is prescribed in doses of fifteen to twenty grains a day. As a diuretic it possesses some virtue, but beyond this quality it does not seem to exhibit any special efficacy that is not equally manifested by the well-known and oftentried remedies that have been already enumerated.

The hydropathic treatment of the gouty diathesis has been mentioned upon a preceding page. Similar measures have been advo-

cated in the local treatment of the acute disease. Hippocrates and his pupils were familiar with the relief from pain that may be procured by immersion of the affected limb in cold water. The illustrious Harvey, discoverer of the circulation of the blood, is said to have followed this practice in his own case, and yet to have reached a great age. In later years the affusion of cold water, followed by cold compresses laid upon the inflamed joint, has found advocates. But Sir A. Garrod, whom nothing has escaped, found that this practice was by no means uniformly successful in the relief of pain. Such alleviation of suffering as may have been experienced was merely transient, and was followed by a renewal of agony so soon as the cold applications were discontinued. The chief objection to the practice lies in the fact that in many instances the suppression of local inflammation by cold is followed by violent invasion of the internal viscera. The stomach, the heart, and the brain may be thus attacked by an inflammation that has been driven from the periphery, where it was comparatively harmless, to the central organs of the body where its manifestation must be accompanied by the most serious risks.

The same objection can be urged against the application of leeches to an inflamed joint. Garrod and his associate, Todd, have noted the interesting fact that after such local depletion joints thus treated remain permanently weakened, and may even become completely ankylosed. Before the days of aseptic surgery there was also no little danger of erysipelas and other infections through the cutaneous wounds that were thus inflicted.

During the period when every one was experimenting with anæsthetics, lotions and sprays of ether and chloroform were sometimes prescribed. To the refrigeration of the affected parts by a rapidly evaporating lotion or spray, the same objection should be raised that is laid against the application of cold water—there is danger of causing retrocession to the internal viscera of the body. But to the use of chloroform as a counter-irritant and anodyne in association with the ordinary narcotic liniments, there can be no reasonable opposition. During the stage of convalescence a well-fitted bandage is often of service; and sometimes a tardy subsidence of local œdema may be accelerated by the application of a blister.

Retrocedent Gout.

Retrocedent gout requires prompt and energetic treatment. The transfer of symptoms is to either the head, the heart, or the gastro-intestinal tract. The indications for treatment are twofold—to obviate the danger of collapse, and to recall the disease to the distal

articulations of the limbs. When the brain is the seat of retrocedent phenomena, the symptoms of coma are rapidly developed. Under such circumstances, if the patient be plethoric, blood should be taken from the arm to the amount of ten or fifteen ounces. Some of these cases are really due to uræmia, and bleeding is in such as useful as it is in puerperal eclampsia. Blood-letting should be followed by a drastic purge with calomel and jalap, or with croton oil if there be difficulty of deglutition. Mustard poultices should be applied to the extremities, in order to provoke the return of inflammatory action about the deserted joints.

When metastasis to the heart or stomach has occurred, the prominent symptoms are those of collapse. Hypodermic injections of ether (ten drops every few minutes) are very efficient for the stimulation of the heart. Whiskey and hot water may be given by the mouth, or by injection into the rectum if the patient cannot swallow or retain the potion. Small and stimulant doses of laudanum—one or two drops every ten minutes—are also beneficial, especially if given with the aromatic spirit of ammonia. Sinapisms, or even a blister, should be applied over the stomach and to the extremities, and the patient should be thoroughly warmed with bottles and rubber bags filled with hot water, and wrapped with flannel, to prevent vesication of the skin. The flatulence that is so often present may be relieved by camphor, or the oil of cajeput, or hot peppermint water with compound tincture of cardamom seeds. In mild cases of gastric disturbance occurring in chronic gout this form of gastric stimulant may be often sufficient, but in the grave cases of metastasis the most energetic treatment is required. If these efforts are successful and the articular manifestations reappear, the patient will for several days need a light diet and the treatment that is appropriate for inflammatory conditions of the stomach and bowels. Colchicum may then be administered in small doses for a considerable period of time.

Chronic Gout.

The treatment of chronic gout consists, for the greater part, in the general treatment of the arthritic diathesis according to the methods that have been already considered. But the different forms in which the chronic disease is manifested require certain corresponding variations in the treatment. Sometimes the general health remains good despite the fact that the joints become stiffened by gradual infiltration with urate salts. In such cases it is not unusual to experience intermittent attacks of articular inflammation; but the severity of such exacerbations is ordinarily less than in acute

gout. In other cases, the local manfestations about the joints are comparatively insignificant, but the force of the disease is expended upon the respiratory organs, the circulatory apparatus, or the kidneys. Obviously, these patients require a form of treatment that is adapted to the special disorder of the internal viscera, while for those who belong to the other class a different method will be applicable.

For the class of patients in whom chronic articular manifestations predominate, a long-continued course of intermittent alkaline medication yields the best results. The carbonated salts of lithium or of potassium, or the salicylate of sodium, may be given in small doses during one-half of each month. When the last-mentioned salt is administered, it should be given in five-grain tablets before each meal and at bedtime, with fifteen drops of dilute nitro-hydrochloric acid shortly after the meal. These remedies are especially useful when painful sensations are experienced in the abdominal and pelvic viscera, or if neuralgic headache be a prominent symptom. If there be any tendency to the passage of gravel, the patient should be instructed to drink Apollinaris water, or the waters of Vals, Royat, Pougues, Contrexéville, Bath, Buxton, Clifton, Poland, or Waukesha. For those who cannot afford the natural spring waters, the distilled waters that are now prepared on so large a scale for the manufacture of ice, or even the condensed steam from an ordinary boiler, may be recommended. During one-half of each month the patient should endeavor to dispense with the use of drugs, in order to prevent the establishment of tolerance, or of debility from too long persistence in the employment of alkalies. At all times, however, the rules of hygiene and exercise must be observed, together with all the precautions in the way of diet and occupation that have been already inculcated. When the season of the year is favorable, a sojourn at some one of the numerous hot springs, for the purpose of a systematic course of warm baths, will be found advantageous. Warm bathing conjoined with massage at home is always very beneficial.

When the digestive organs are in a fairly good condition, iodide of potassium, in doses of two grains three times a day, often exercises a salutary effect, hindering the formation of deposits about the joints. The administration of the drug should be occasionally suspended for a fortnight at a time, to prevent the establishment of tolerance on the part of the tissues. Colchicum may be in like manner exhibited in small doses for considerable periods of time. In one instance the late Sir Henry Holland administered this remedy for two years with decided benefit to the patient. Usually, however, it is advisable to reserve its use for the relief of the painful exacerbations that diver-

sify the course of chronic gout. So great is the comfort that is derived from its exhibition on such occasions, that the risk of tolerance through constant use should be avoided. Still, there are many experienced physicians who do not fear the continuous administration of colchicum provided the dose be small enough to obviate all danger of gastro-intestinal irritation and cardiac depression. Thus employed, many of the headaches, backaches, irritative coughs, and other symptoms of gouty disorder may be kept at bay.

One of the most universal consequences of chronic arthritic toxæmia is an impoverished state of the blood. The death and insufficient reproduction of the red corpuscles are constant results of the presence of the nitrogenous toxins. Bitter tonics—quinine, strychnine, quassia, gentian, and calumba—are useful, and, if there be no considerable catarrhal inflammation of the gastro-intestinal mucous membrane, iron may be given. The ferrated mineral waters then fulfil a valuable indication. But if the patient cannot tolerate iron, arsenical preparations form the best substitutes. The waters of Royat, Orezza, and of the Mt. Shasta arsenical springs in California, have a good reputation in such cases. Or the liquor potassii arsenitis may be given in moderate doses for a long period of time. The ordinary stimulants, tea, coffee, and alcohol, which usually are not tolerated in chronic gout, can be sometimes administered for a few days at a time to these feeble subjects when they experience the need of a cardiac stimulant. In many instances laxatives are required. Among the best for anæmic patients is guaiacum, which can be administered in capsules or wafers or effervescing powders in order to obviate its disagreeable taste. Cascara is also a valuable laxative. The combination of sulphur and cream of tartar in tablet form is a very gentle and elegant remedy in cases of hemorrhoidal tendency with torpor of the liver and kidneys. An occasional purgative course of blue pill, colocynth, colchicum, and hyoscyamus is advantageous. When atonic dyspepsia is a conspicuous symptom, the simple bitters, quassia, calumba, nux vomica, gentian, and euonymin are beneficial. Associated with rhubarb they are useful in cases of intestinal atony. Sydenham was in the habit of prescribing for such patients an electuary composed of various mints, horseradish, mustard, and bitter herbs. This was supplanted during the next century by a mixture of bitter and aromatic powders derived from the vegetable kingdom and rendered fashionable by the affix of the aristocratic title of the Duke of Portland. In comparatively recent times Sir Alfred Garrod has endeavored to popularize the following prescription, which is also indorsed by Sir Dyce Duckworth:

℞ Pulv. resin. guaiaci ..... ʒ vi.
Pulv. cinchonæ flavæ ..... ℥ i.
Ammonii carbonat ..... ʒ ij.
Potassii (vel Lithii) citrat ..... ʒ ij.
Potassii iodidi ..... ʒ i.
Pulv. colchici rad ..... ʒ i.
M. et ft. pulvis. Sig. Forty grains for a dose in a wineglassful of peppermint water to be taken once a day, continuously or in alternate weeks.

All such preparations have for their common object a gentle stimulation of the circulation and of the excretory functions.

When the renal complications of chronic gout become predominant it is necessary to avoid the use of colchicum, and to restrict the patient to a milk diet. This constitutes the surest means of retarding the progress of nephritis, and of obviating the mal-assimilation and semi-starvation that are inevitable when ordinary food is allowed. Tonics and astringents may be administered, but their utility is often open to suspicion. The excretory action of the skin and intestinal tract should be stimulated by hot-air baths, counter-irritation over the loins, and hydragogue cathartics.

Many cases of chronic gout are terminated by failure of the heart to maintain the circulation. So long as compensatory hypertrophy of the ventricle persists, the blood will be efficiently propelled; but when the ventricular tissues begin to yield, so that dilatation of the cavities occurs, stagnation commences, and the protracted agony of death at the heart is initiated. At first, great relief may be obtained by the use of digitalis, but this drug soon disorders the stomach, rendering it necessary to have recourse to sparteine, strophanthus, and convallaria. These remedies in their turn cease to relieve and then temporary benefit can be procured from caffeine. Milk, either with or without coffee, forms the best nourishment, and is the diuretic that can be for the longest time endured by the kidneys. Taken in the form of an effervescent kumyss it is usually agreeable and always efficient. Small doses of blue pill or of calomel are often prescribed, and the liver should be sufficiently drained by the aid of saline laxatives. In advanced cases, the application of sinapisms or flying blisters over the precordial region may relieve pain and aid the circulation for a brief period. Hot whiskey and water and hot coffee also act as palliatives when cyanosis and other evidences of stagnation are apparent. But all these measures fail at last, and when their need is urgent the end is near.

Besides the general management of chronic gout that has been already described, it is a matter of great importance to prescribe energetic local treatment for the joints that have been the seat of uratic

deposits. The articular rigidity and disorganization that result from such incrustations serve to cripple and to disable the patient even more than is effected by the conditions that accompany the acute attack. It is, therefore, desirable to hinder the process of infiltration with uratic salts, and to promote their absorption and removal when they have already been deposited. It has been shown that the feeble circulation of blood and lymph in the substance of the articular structures is one of the causes that determine the precipitation of urates in the tissues rather than elsewhere. For this reason the principal indication for local treatment is to quicken the circulation of blood in the affected parts. This can be accomplished by hot fomentations reinforced with turpentine, mustard, oil of sassafras, and other aromatic substances and essential oils. The various liniments that contain ammonia, camphor, menthol, oil of cajeput, and similar ingredients, are all rubefacient, and consequently beneficial. Friction of the surface with coarse towels, hair gloves, and flesh-brushes, operates in a similar manner. Steaming the affected parts, or even the entire body, with terebinthinate vapors from pine needles and cones, or from the berries of the juniper bush, has had its advocates. Copious perspiration induced by the Turkish bath is beneficial, and may be frequently encouraged if the heart and kidneys are intact. Massage of the stiffened joints is very useful to counteract the development of rigidity. The manipulation of the joints should be performed in a warm bath, for the reason that the process of resolution is aided by the local application of heat in connection with movement of the stiffened parts. For the same reason the patient may be advised to visit the various hot springs, especially those sources whose water is charged with sulphur. Of comparatively little value in the acute forms of gout, these waters are decidedly beneficial in the local treatment of the articular and cutaneous disorders that occur in the chronic variety of the disease. Chief among the American springs that are adapted to this purpose are the hot sulphur springs among the mountains of Virginia, and at Glenwood in Colorado. The hot springs of Arkansas, and of South Dakota, Idaho, and the Yellowstone Park, are principally useful by reason of their very efficient thermal qualities. But when the rigid joints cannot be relaxed by such measures, it becomes necessary to apply strong tincture of iodine or flying blisters of cantharidal plaster, or even to cause superficial vesication of the skin by a few strokes with the actual cautery lightly applied in the vicinity of the stiffened articulations.

Sometimes it happens that elderly patients exhibit a persistent œdema involving the extremity that has been the seat of gouty inflammation. This complication causes considerable disability and

pain, and is often very refractory under treatment. It is due to a paretic condition of the local vasomotor nervous apparatus, and requires the employment of the various topical applications that have been already specified. If the œdema be not occasioned by renal or cardiac disease, these measures will often prove successful. But if they fail it may be well to apply a flannel bandage, or an elastic stocking, for the support of the vessels. The application of flying blisters and the actual cautery may be reserved for extreme cases.

The fact that in many instances the uratic deposits very nearly approach the cutaneous surface, has raised the question of surgical interference for their removal. In the majority of cases, however, this will be either unnecessary or positively injurious. Superficial deposits, such as are often visible upon the ears and in the skin, sometimes excite ulceration of the overlying cuticle, and thus evacuate themselves. Occasionally a subcutaneous bursa spontaneously discharges its contents and must be treated like any other abscess. If such fistulous openings cannot be freely incised and cleansed, recourse must be had to compresses wet with alkaline solutions and covered with oiled silk or a rubber bandage. Such lotions should consist of potassium bicarbonate, or potassium iodide, or lithium carbonate, to the amount of sixty or eighty grains in a pint of water, which may be agreeably perfumed if the patient be of sufficiently exalted rank and wealth. When large concretions have formed in and around certain joints, ulceration sometimes occurs, and the tophi are spontaneously extruded. This process is sometimes witnessed at the knuckles and phalangeal joints. Various surgeons have attempted to anticipate or to assist this effort by making free incisions and endeavoring to turn out the mineral masses that interfere with articular movement. Careful scraping of the bones and curetting of the cavities of the joints, followed by antiseptic dressings, may sometimes be accomplished with some degree of benefit to the patient. But in the majority of cases it is better to abstain from all surgical measures, and to seek relief by the methods that have been already described. The same opinion must be entertained regarding the employment of electricity. If it does no harm it is very doubtful whether it can effect anything more than temporary alleviation of pain in a few cases of acute gout.

Treatment of the Obscure Manifestations of the Gouty Diathesis.

We have seen that the gouty diathesis, or, in other words, attenuated gout, is usually manifested by a considerable number of disorders involving the different organs of the body, sometimes long before

the occurrence of articular crises. These disorders, when dependent upon the diathetic condition of the patient, require certain modifications of treatment, just as the diseases that occur in malarious subjects are modified by the action of malaria, and require special treatment with reference to the underlying complication.

The *nervous system* always suffers from the toxic influences of gout. In the latent form of the disease the patient is often greatly depressed in spirits, moody, fretful, or surly. The melancholic varieties of insanity may be experienced, and they often persist until cured by a sudden outbreak of articular gout. In all such cases, efficient elimination is needed. The diet must be regulated so as to contain a minimum of meat, and active exercise must be maintained. If the heart is not seriously affected, a mercurial purge, followed by a course of alkalies, sodium salicylate, or even colchicum may be administered. In cases of insomnia, the same general treatment must be employed. A foot-bath, and a full dose of potassium citrate or of lithium citrate in a glass of hot lemonade at bedtime, are to be preferred to narcotics of all kinds.

Epilepsy is often accompanied by symptoms that are due to the accumulation of nitrogenous toxins. A diet of vegetables, milk, and fish may be allowed. The digestive organs require careful supervision. Alcoholic stimulants and venereal excesses must be forbidden. An occasional mercurial cathartic is beneficial, and the specific treatment with bromides should be supplemented with other alkaline salts, alternately with sodium salicylate.

Ordinary gouty *headaches* require the general treatment that is appropriate to the diathetic condition. *Hemicrania* is usually treated with mercurial carthartics, antipyrin, caffeine, and alkalies. A glass of wine and a good dinner sometimes give prompt relief, a fact that Haig explains by their action in driving uric acid and its congeners out of the blood into the tissues. But the suppression of pain that is thus effected has to be paid for by subsequent misery when the accumulated refuse re-enters the current of the circulation. The treatment that is at the same time palliative and curative consists in the administration of five or ten grains of sodium salicylate before each meal, with a dose of fifteen or twenty minims of dilute nitrohydrochloric acid after the repast. General treatment for the improvement of the health is also desirable.

Neuritis of gouty origin, though not very common, is exceedingly persistent. It is often dependent in part upon alcoholism induced by the habits of the patient. It requires a long course of potassium iodide and quinine—three grains of the former with one grain of the latter, three times a day. If the bowels are constipated, a few

drops of tincture of colchicum seeds may be added. Counter-irritation over the affected nerve should be maintained with cantharides, or tincture of iodine, or a mixture of equal parts of chloral hydrate, camphor gum, and menthol. The galvanic current along the course of the nerve for five minutes every day or two is a valuable adjuvant to the general treatment, as it is also in *neuralgia*, an affection that requires essentially the same treatment that is requisite for neuritis. It is best to avoid as far as possible the use of hypodermic injections of morphine, but sometimes they must be employed, in order to secure rest from the wearing pain. In such cases, especially when the sciatic nerve is involved, the propriety of surgical intervention by nerve-stretching or nerve-section should be considered.

Vertigo is not infrequently experienced by the gouty patient. It is often temporarily cured by an attack of articular gout. An occasional mercurial cathartic, and relaxation of the bowels with rhubarb and magnesia at bedtime, together with a dose of compound tincture of gentian and potassium acetate before each meal, will usually effect a cure. If these remedies fail, colchicum may be given in moderate doses for a number of weeks or months. A similar course is indicated when *muscular cramps* in the calves of the legs, or elsewhere, become annoying.

The tedious attacks of *bronchitis* that harass the gouty subject have been fully discussed. In addition to the ordinary expectorant, anodyne, and antispasmodic treatment of the bronchial affection, the use of potassium iodide, colchicum, and arsenic is indicated. When *asthmatic symptoms* predominate, the bowels should be kept freely open, and the ethereal tincture of lobelia in doses of fifteen or twenty minims may be added to the ordinary expectorant mixture. Potassium iodide is also indicated unless there be a bronchorrhœa by which the lungs may be flooded. In such cases terpine hydrate or the compound tincture of benzoin will be found useful. The fumes of nitre and stramonium leaves are useful on condition of being inhaled in large volumes. The addition of tobacco is often beneficial, and the mixture may be smoked in a pipe or in the form of a cigar. The English praise the following mixture:

℞ Pulv. fol. stramonii..... ℥ ss.
Pulv. anisi,
Potass. nitrat.....āā ʒ ij.
Pulv. fol. tabac.....gr. v.
M. et ft. pulvis. Sig. A teaspoonful to be burnt in a saucer, and the fumes to be inhaled.

Chloroform, ether, and chloral hydrate often give great relief, but tolerance is soon established. The same thing may be said of

morphine. In desperate cases a change of air will often effect an immediate cure even when death had seemed imminent.

The disorders of the *heart* have been already considered, but certain symptoms connected with the circulatory apparatus demand further attention. Gastric disturbances are frequently acccompanied by excessive pulsation in the large arteries of the body. This sometimes causes intolerable throbbing in the head, usually in one of the temples. The general treatment of arthritism and of chronic catarrhal dyspepsia is indicated. Elimination and tonic treatment are the first indications. Tincture of aconite has been recommended against the inordinate pulsations, but its effect is inferior to that of sodium or strontium bromide in moderate doses. After the catarrhal symptoms have been somewhat reduced, a course of nitro-hydrochloric acid and bitters is useful. Intermittent or irregular pulsation of the heart is usually dependent, when no organic disease can be discovered, upon chronic intoxication with nitrogenous toxins, and it is best treated by correction of the diet, mineral waters, sulphur or guaiac laxatives, occasional doses of blue-pill and colocynth, and the mineral acids with bitter tonics. A course of sodium salicylate often effects great benefit. Similar measures are needed in cases of *cardialgia* after the acute neuralgic pain has been subdued by emptying the cavity of the stomach with a lobelia emetic or with the gastric siphon, followed by the administration, every fifteen minutes, of drachm doses, properly diluted, of equal parts of aromatic spirit of ammonia and spirit of chloroform. Sometimes the severity of the pain requires a hypodermic injection of morphine and atropine before anything else can be done. When the heart is organically diseased, and the coronary arteries are incapable of fully conveying blood to the cardiac walls, genuine *angina pectoris* may occur, often with a fatal result. Inhalation of amyl nitrite, and the administration of nitroglycerin tablets (gr. $\frac{1}{100}$) every ten or fifteen minutes, will be necessary in addition to the other measures above mentioned.

Hemorrhages from the veins of the rectum and nasal passages are not uncommon events among the gouty. They are frequently beneficial, and require only the ordinary treatment, with proper regulation of the diet and attention to the excretions. Epistaxis sometimes occurs in elderly persons who have never experienced such a flux in earlier life. It is then usually the consequence of latent arthritic conditions, and is followed by the same relief that is obtained after an articular crisis. Occasionally such patients discharge blood from the fauces or bronchi. The color of the expectoration is dark. Speedy relief is procured by the application of a few leeches around the anus.

Phlebitis occurring in a gouty subject requires the usual local

treatment for inflammation of the veins. Warm fomentations narcotized with belladonna or the oleate of morphine may be applied over the affected vessel, and the limb should be kept at rest. Vegetable food and the general treatment of the arthritic diathesis should be prescribed for several months. The action of the heart must be properly sustained with quinine, strychnine, and the mineral acids as acute symptoms subside. Sometimes the affected limb remains more or less persistently œdematous after the cessation of active inflammation. Warm douches, friction with the hand, and an elastic stocking are the best remedies for this condition, but they must not be prescribed until all danger of detachment of fragments from the clot has disappeared.

The sockets of the teeth are sometimes attacked by a chronic inflammation—*pyorrhœa alveolaris*—that results in absorption of the alveoli, followed by the falling out of the teeth. This malady usually occurs among arthritic subjects, and is an indication for the adoption of measures that are appropriate to that predisposition.

Lingual neuralgia is usually experienced during the winter, and often vanishes with the appearance of fresh fruits and vegetables, in the spring.

Leucoplakia is sometimes due to similar causes, but is a more obstinate affection. It should be treated with non-poisonous antiseptic lotions, and the white patches on the surface of the tongue should be touched as often as once a week with a saturated solution of chromic acid, or with a one-half of one per cent. solution of the bichloride of mercury.

During the first twenty-four hours of its course *tonsillitis* may be sometimes aborted by the administration, every three or four hours, of five grains of powdered guaiac with half a drachm of potassium bicarbonate in a wineglass of lemonade. Sodium salicylate may be given in ten-grain doses every two hours until the acute symptoms begin to subside. The subsequent treatment should be adapted to the arthritic predisposition of the patient.

The *biliary disorders* that accompany gout are usually of a functional character unless chronic alcoholism also exists. Constipation, headache, hemorrhoids, lassitude, and depression of spirits are among the most conspicuous symptoms. They demand the employment of the measures that have been already described—mercurials with colocynth and colchicum, saline cathartics, especially those that contain sodium sulphate, the mineral waters, and, in the later stages of the disorder, mineral acids and bitter tonics.

Renal disorders connected with arthritism have been already sufficiently described. Certain affections of the genital organs may be

noted as usually dependent upon the gouty diathesis. Of these, *balanitis* and *herpes prepatialis* are not uncommon. They can be usually arrested by the application of listerine or other similar lotions containing boric acid, eucalyptol, and menthol. In severe cases it may be necessary to dust the parts with boric acid, and to insert a piece of lint between the glans penis and the prepuce. *Pruritus of the vulva* requires essentially the same method of treatment. When dependent upon glycosuria, great attention to cleanliness, alkaline injections, borated lotions, mercurial ointments, and cocainized salves are indicated. *Priapism* of a persistent character sometimes torments elderly gouty subjects. Efficient elimination and the continued use of potassium iodide will generally give relief. Sometimes an attack of *orchitis* occurs as a manifestation of acute or retrocedent gout. Its treatment must be conducted in accordance with the general principles that have been already enunciated. The same thing may be said of the non-venereal *urethritis* and *prostatitis* that are sometimes experienced. Severe attacks of *cystitis*, occasionally accompanied by vesical hemorrhage, are not infrequent. They are sometimes connected with the recession of an eczematous eruption from the skin. Rest, milk diet, copious draughts of linseed tea, infusions of buchu, uva ursi, triticum repens, or slippery-elm bark, with largely diluted solutions of potassium citrate, or lithium citrate, should occupy the patient during the acute stage of the disease. Londonderry lithia water and the waters from the Poland or Waukesha springs are very grateful beverages. Opiates and the solanaceous extracts are needful for the relief of pain. Colchicum and mercurial laxatives are required at intervals.

Many cases of *dysmenorrhœa* and *pelvic neuralgia* are dependent upon the arthritic diathesis for their existence. Much unnecessary gynecological surgery might be avoided were this fact more generally appreciated. In addition to the general treatment, cannabis indica, potassium bromide, phenacetin, salol, or sodium salicylate may be used for their anodyne effect. Atonic constipation with universal torpor of the circulation is greatly benefited by the daily use of guaiacum in laxative doses. Hepatic torpor and hemorrhoidal tendencies may be counteracted by the long-continued daily administration of sulphur and potassium bitartrate in tablet form. Iron, quinine, strychnine, and arsenic should be given at the same time in order to increase the stability of the nervous system. Daily bathing in warm water should be practised, and, if possible, the patient should be encouraged to seek a change by periodical visits to the various hot springs in Virginia, Arkansas, South Dakota, and the Rocky Mountains.

The different cutaneous diseases that occur among the gouty—pruritus, psoriasis, eczema, urticaria, and herpes—all require the same recognition and treatment of their common diathetic basis. Their management will be fully considered in the volume on diseases of the skin, and may be briefly summarized as consisting of appropriate elimination, anodyne local applications, general correction of the functions of digestion, assimilation and metabolism, together with a chronic and mildly arsenical medication of the nervous system. Residence at a distance from the ocean, the prolonged use of warm baths, and abundant exercise in dry bracing air, are to be enumerated among the most efficient remedial measures.

For the treatment of the different forms of lithiasis which so frequently accompany gout, the reader is referred to the volumes of this work that treat of renal and hepatic diseases.

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ARTHRITIS DEFORMANS.

BY

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ARTHRITIS DEFORMANS.

Introductory.

The defects and shortcomings of the system of classification of diseases, which is of necessity adopted, in default of a better, in the text-books of medicine of the present day, is nowhere more manifest than in connection with those diseases in which joint affections play a conspicuous part. It is customary to group together, as diseases of the joints, a series of systemic maladies which have little in common with each other beyond the tendency to involve the articular structures. It is true that the diseases so included present superficial resemblances, and have indeed been at all clearly differentiated only in comparatively recent times. The first step that was made in this direction was the separation from gout of the disease which is now known as rheumatism, and it was not until many years later that there was recognized a third disorder which had previously had no distinct place in medical literature, but was confused now with gout and now with rheumatism, according to the views which prevailed at various times and in various places, as to the boundaries of the provinces of those two disorders.

Even at the present day there are many who hold that after all gout, rheumatism, and arthritis deformans are much the same thing; and the want of stability in the notions which still prevail is reflected in our nomenclature, for arthritis deformans enjoys the distinction of having been called by a larger number of different names than any other in the whole catalogue of diseases. In England it is most frequently spoken of as "chronic rheumatic arthritis," "osteo-arthritis," or "rheumatoid arthritis." In France the name of "rhumatisme noueux" is perhaps most frequently employed; while in America and in Germany that of arthritis deformans, which will be employed in the present article, has been widely adopted. This last name, originally suggested by Virchow, is preferable to most of the others which have been proposed, for it implies no theory and presupposes no relationship to other maladies, but merely records the most conspicuous feature of the disease; however, it possesses the disadvantage which is not shared by osteo-arthritis, a name which

is equally free from objection in the above respects, that it has a forbidding sound and a gloomy prognostic significance.

Although, as we have seen, our knowledge of arthritis deformans as a distinct disease has had such recent beginnings, the history of the disease itself can be traced back, in a fragmentary manner, it is true, to a very remote period of antiquity, much further indeed than that of any disorder which confines its ravages to the softer structures of the human body. Bones bearing the unmistakable stamp of this disease have been unearthed by Professor Petrie[1] in the course of his explorations in Egypt, and some of the bones so marked, which he has found, date back in all probability to the very dawn of Egyptian history, while others which have been described by Eve[2] were probably those of persons who lived not earlier than the Ptolomaic times.

Similar evidences have been met with by Delle Chiage, in bones found among the ruins of Pompeii, by Norman Moore[3] in the bones of a skeleton discovered in a Roman sarcophagus in London; and by Virchow[4] in those from the graveyard of an ancient convent in Pomerania which was founded in the year 1356.

Nor were the characteristic features of arthritis deformans overlooked by the older medical writers, as may be gathered by passages embodied in the works of Sydenham, Musgrave,[5] de Sauvages,[6] Haller,[7] and others. Sydenham's[8] account is particularly worthy of notice. When speaking of the sequelæ of rheumatic fever he describes as an occasional legacy of that disease a condition of the joints which may persist for years or even throughout the life of the patient, characterized by distortion and deformity with nodular outgrowths of the finger-joints and other articulations, which tend to cripple the sufferer more or less completely, although his general health may remain little if at all impaired.

Passing on to more modern times we find that the honor of having first differentiated arthritis deformans is shared by a French and an English physician, to the former of whom we owe the first description of the peculiarities of its morbid anatomy, while to the latter is due the credit of having first recognized clearly its distinctive clinical features.

From the writings of French physicians at the end of the eighteenth and beginning of the nineteenth century it may be gathered that cases of the disease under consideration were at that period usually classed as examples of gout, whereas in England the tendency was rather to include them in the rheumatic group.

On the 16th day of Thermidor, in the year VIII. of the French Republic (August 3d, 1800), there was read before the faculty of Paris a thesis by Landré Beauvais,[9] on a form of joint disease to which he

assigned the name of "Goutte Asthénique Primitive," and it has been claimed by Charcot for this thesis that it embodies the earliest description of arthritis deformans as a distinct morbid entity. This claim is to a great extent justified by the fact that Landré Beauvais certainly described the changes which this form of arthritis produces in the structures of the joints which it attacks, such as the destruction of the articular cartilages and the enlargement of the articular ends of the bones, apart from any deposit of tophaceous material. Yet when we consider the clinical descriptions of cases contained in this thesis, it is impossible to suppose that more than a comparatively small proportion of the cases included were actually examples of arthritis deformans; some were certainly examples of true gout, and others were of very doubtful nature.

One rises from the perusal of the work of Landré Beauvais with the impression that while the honor of first recognizing the morbid changes due to arthritis deformans belongs without question to this observer, his ideas as to the clinical phenomena corresponding to such lesions were extremely vague.

Heberden,[10] writing in 1804, was sufficiently alive to the distinctive features of the disease to suggest that it ought to be separated from both true gout and true rheumatism; and he first described the small nodular outgrowths upon the terminal joints of the fingers which are universally known as Heberden's nodes.

The following year (1805) saw the publication of Haygarth's [11] classical monograph on "Nodosity of the Joints," a purely clinical essay, in which the author describes his experience of the disease under consideration, during many years of practice as a physician at Bath.

The series of thirty-four cases upon which he based his conclusions sufficed to enable him to observe and describe many of the more striking clinical features of the malady. Speaking of the manner in which his attention was first drawn to this subject, Haygarth says: "A case happened to occur to my observation at a very early period which, compared with others at subsequent times, convinced me that there is one painful and troublesome disease of the joints, of a peculiar nature, and clearly distinguishable from all others by symptoms manifestly different from the Gout, and from both acute and cronick Rheumatism."

Haygarth remarked upon the peculiar liability of the female sex to this disease, especially at or about the period of the menopause; the special tendency of the joints of the fingers to be attacked; the characteristic enlargement of the articular ends of the bones, and the essentially chronic nature of this malady which tends to involve

one joint after another, until the patient may be crippled by it; and which as it spreads has no disposition to relinquish its hold upon the articulations which have suffered previously.

It would appear that Haygarth's views did not meet with general acceptance among his contemporaries, and for some years after the publication of his essay there is an almost complete blank in the literature of the subject. Even Scudamore[12] in his work on Rheumatism, which was published in 1827 (twenty-two years after Haygarth's paper), although he refers to the observations of Haygarth, says that he has seldom met with the condition described by that author except as a consequence of antecedent attacks of gout or rheumatism. Brodie,[13] on the other hand, maintained that this disease differed essentially from both those maladies.

The study of the morbid anatomy of arthritis deformans, initiated as we have seen by Landré Beauvais, was vigorously pursued by a number of observers both on the Continent and in the British isles, and among these Cruveilhier,[14] Lobstein[15] and Aston Key,[16] Adams[17] and Robert Smith[18] of Dublin, Canton[19] and Deville[20] and Broca[21] must be especially mentioned. It is to the researches of Adams and Robert Smith that we owe the recognition of the fact that the disease of the hip-joint met with in elderly men, which so frequently has its origin in an injury, slight or severe, is in its essential nature identical with the disease of many joints, both small and large, to which women are specially liable.

There is probably no institution which provides a richer field for the study of arthritis deformans than the Salpêtrière in Paris; and it was from this institution, upon which the brilliant researches of Charcot have conferred a world-wide celebrity, from the pen of Charcot[22] himself, then an interne, and from that of his colleague Trastour[23] that the next important contributions to the study of this disease emanated. The graduation theses of these authors and that of their contemporary Vidal[24] supply, indeed, a most comprehensive account of its clinical aspects.

Both Charcot and Trastour maintained the view that arthritis deformans is merely a variety of chronic rheumatism—an opinion which was very widely held by French physicians, at any rate up to a very recent period, and which still finds distinguished adherents, among whom may be mentioned Dr. Mitchell Bruce who has contributed the article upon this subject in Quain's Dictionary of Medicine, and the late Professor Kahler of Vienna. One of the most interesting portions of Charcot's thesis is that in which he describes and classifies into definite types the deformities of the hands which result from the

changes in the joints, and from the spasm of the muscles which control the movements of the fingers.

The view that arthritis deformans is a distinct disease differing in its pathology from both rheumatism and gout was vigorously upheld in England by Fuller[25] and Garrod,[26] whose works, published in the years 1852 and 1859 respectively, contained accurate descriptions of the disease. Both authors urged in support of their opinions the fact that the visceral manifestations of true rheumatism are not met with in the disease under consideration, and Garrod showed that the presence of an excess of urate in the blood which he had demonstrated to be a feature of true gout was not to be detected in cases of arthritis deformans.

Of more recent years the study of arthritis deformans has been approached from many sides by a number of observers, and the prevalent views as to the nature both of this disease and of true rheumatism have undergone and are still undergoing profound changes; moreover the gradual displacement of the older chemical theories of true rheumatism, by the growing belief that that disease is due to a micro-organism still unrecognized, has tended to draw more distinctly than ever the line of demarcation between them.

The view is now widely held that the nearest allies of arthritis deformans are to be found in the joint lesions which are associated with gross diseases of the nervous system; and this opinion receives powerful support from the undoubted and close resemblance between the morbid changes in the joints to which it gives rise, and those met with in the joints of patients suffering from locomotor ataxia and who have developed the so-called Charcot's disease.

It is but a single step further to suppose that arthritis deformans is itself a disease of nervous origin, and that the joints which it attacks become subject to dystrophic changes; and the hold which this theory has gained upon medical opinion is in great measure due to the writing of Senator[27] and R. Wichmann[46] in Germany, Ord[28] and Duckworth[29] in England, Weber[30] in America, to mention only a few of the authors who have dealt with this aspect of the question. Another view which must be mentioned, and of which Hutchinson is the leading exponent, looks upon arthritis deformans as neither a distinct disease nor a variety of gout or rheumatism, but as the product of a blending of gout and rheumatism, in which now the one and now the other element preponderates.

Arbuthnot Lane[31] and others ascribe a large share in the causation of the lesions to mechanical wear and tear of the joints; while some believe that in its most chronic forms the disease is largely of the nature of a senile change.

It will be seen then that we are very far, at present, from arriving at any degree of unanimity as to the nature, and consequently as to the proper treatment, of arthritis deformans; and that the theories as to its nature which have been propounded are only less numerous than the names which have been assigned to the disease.

He who endeavors to write a consistent account of arthritis deformans is met at the outset of his task by the difficulty that under this name are included cases which differ widely from each other in their clinical aspects, so widely indeed that we should almost be justified in regarding them as examples of distinct disorders, were it not that the morbid changes in the joint structures are of like nature in all. Hence it is that one is driven to take these changes as the sole criterion of the nature of the case, and to classify all cases in which they occur as examples of arthritis deformans.

Morbid Anatomy.

Seeing that the changes in the articular structures which result from arthritis deformans have been carefully studied by a long series of able observers, our knowledge of these changes, at any rate in their more advanced stages, is tolerably complete. All the tissues which enter into the structure of the joints, viz., cartilage, bone, and synovial membrane, share in the morbid process, but it cannot even yet be stated with certainty which of these structures is first attacked, although there is a great probability that the cartilaginous coverings of the articular ends of the bones are the actual primary seats of the disease.

This uncertainty is not a matter for surprise if it be remembered that arthritis deformans is not in itself a fatal malady; and consequently that it is only very occasionally and, so to speak, accidentally that an opportunity is afforded of examining the joints in the earliest stages of the disease.

It cannot be contended that the observed changes are absolutely characteristic of the cases to which the name of arthritis deformans is usually applied, for similar lesions are met with in the joint disease of locomotor ataxia, in that which occurs in hæmophilia, as well as in gouty cases of long standing. Even among the cases commonly classed together as examples of arthritis deformans there exist conspicuous clinical differences, such as separate the hip-joint disease of elderly men from the more acute affection of many joints which is unfortunately so common among women; sometimes again it seems that arthritis deformans developing late in life and running a very slow course is little more than a senile change in the joints.

In describing the morbid anatomy of the disease under consideration it will be well to consider the changes in the several articular structures separately, and to describe in turn the fibrillation and erosion of the cartilages; the eburnation and abrasion of the bones, and the outgrowths of new bone around the articular surface; and lastly the hypertrophy of the synovial fringes and other lesions of the synovial membrane.

The cartilage lesions are among the most characteristic of the morbid changes of arthritis deformans. In the early stages of the disease the articular cartilages of the affected joints are seen to have lost their uniform structure, and to present the appearance of velvet; the "nap" consisting of delicate fibrillæ formed from the ground substance of the cartilage, from which the cellular elements have disappeared.

The manner in which the fibrillation is brought about has been carefully studied by Cornil and Ranvier,[32] from whose description the following account is condensed. The earliest morbid appearance observed is the multiplication of the cells throughout the entire thickness of the cartilage, and the formation of capsules around some of them. Within these primary capsules a number of secondary capsules are formed, which may be either independent of each other or grouped together in common envelopes. Previous observers had mistaken these capsules for true cartilage cells, but Cornil and Ranvier showed that this is not their real nature by staining them with iodine, which colors the protoplasm of the cartilage cells brown, but barely imparts a tint to, or altogether fails to stain, these secondary capsules.

The next event is that those primitive capsules which approach most nearly to the surface rupture into the articular cavity, and those which are more deeply seated, being able to grow only toward the surface of the cartilage, rupture into each other, and in this way a series of parallel tubules is formed, and the ground substance of the cartilage is split up into filaments.

The velvety cartilage is before long completely destroyed in places by the friction of the articular surfaces upon each other, leaving the underlying bone completely bare. As might be expected, the removal of the cartilage is first brought about over the central portions of the articular surfaces, but as time goes on the exposed area becomes more and more extensive. As was originally pointed out by Sir James Paget, the remarkable tendency to symmetrical invasion which is so characteristic of arthritis deformans is manifested even in this, and the destroyed area in the joint of one limb may closely correspond both in shape and in position with that in the corresponding

joint of the opposite limb. Rindfleisch holds that the destruction of the cartilage is not purely mechanical, but is greatly facilitated by the process of mucous degeneration, and it is interesting to note, in this connection, that Hoppe-Seyler[33] detected the presence of a large amount of mucin in the synovial fluid removed from a diseased joint.

The changes in the bones in arthritis deformans fall under three heads, viz.:

1. Osteophyte formation;
2. Eburnation;
3. Abrasion.

In contrast to the destruction of the central portion of the articular cartilages already described is the heaping up or lipping of their edges, which is thus explained by Cornil and Ranvier.

The edges of the cartilaginous surfaces are to some extent overlapped and covered by the synovial membrane, and their synovial covering prevents the escape of the contents of the ruptured capsules into the synovial cavity, with the result that the cellular elements collect under it and lead to the formation of outgrowths of newly formed cartilage which are known as chondrophytes. As time goes on these chondrophytes become ossified and then constitute the familiar bony outgrowths or osteophytes which have so important a share in the production of the deformities characteristic of the disease. In some parts, instead of definite outgrowths, a rim of new bone is formed which gives rise to the condition recognized clinically as lipping.

The process of ossification commences, as Volkmann[34] showed, in the parts in the immediate neighborhood of the original bone, and progresses at a slow rate, so that even at a period when the process is far advanced the osteophytes still retain a covering of cartilage. As a result of the outgrowth of osteophytes the bulk of the articular ends of the bones may be very greatly increased, and the mobility of the joint may be thereby seriously interfered with.

Turning to the consideration of the more central portions of the articular surfaces, the bone in these situations also is found to have undergone a remarkable change. The superficial layer has become extremely hard and compact, so that it resembles ivory in appearance, a resemblance which is further increased by the polishing which it has undergone in consequence of the friction of the articular surfaces against each other. On this account the change in question has received the name of eburnation. The smoothness of the eburnated surfaces is broken by minute perforations with which they are riddled, and which correspond to Haversian canals which have been laid open. Eburnation may be regarded as, to some extent, a conservative process,

seeing that the hardness of the ivory-like layer tends to impede the process of abrasion to which the exposed bony surfaces are subjected.

Various explanations of the process of eburnation have been suggested. Thus Ziegler[35] attributes this change to a softening of the subjacent bone simultaneously with the changes in the cartilage which lead to fibrillation, which softening leads to the production of cavities, into which a growth of vascular medullary substance extends, and in this way the formation of a layer of new bone is brought about.

Cornil and Ranvier, on the other hand, ascribe the formation of the compact new bone to the discharge into the adjacent medullary spaces of the cartilage capsules of the deepest layers, which as they increase in size exert pressure upon the intervening bone and so bring about its absorption; but they further admit that inflammatory changes may have a share in the process.

Even the eburnated surfaces often show conspicuous evidence of the abrasion to which they are subjected, and are apt to be scored by deep grooves running parallel with each other and following the direction in which the bones rub upon each other in the ordinary movements of the joint.

By the combined action of the two processes of osteophyte formation and abrasion most profound alterations in the mechanism of the affected joints may be produced. What was originally a convex articular surface may be reduced by abrasion to a concave form, and the abnormal cavity may be rendered much deeper by osteophytic outgrowths surrounding it. There is a specimen in the museum of St. Bartholomew's Hospital (London) which affords a most striking illustration of such changes. In this specimen the shoulder joint is that which is affected, and what was once the glenoid cavity of the scapula has become converted into a highly polished convex boss; whereas the head of the humerus has been changed into a cavity surrounded by bulky osteophytic outgrowths, which have themselves undergone extensive abrasion adapting their form to the requirements of the reversed mechanism of the joint.

Volkmann pointed out that the abrasion of the bony surfaces is almost certainly aided by some alteration in the structure of the bone itself, which in its earlier stages is probably of the nature of a rarefying osteitis; he observed that mere mechanical friction does not sufficiently explain the fact that grooving may take place on portions of the bony surfaces which are not yet denuded of their cartilaginous covering; and he held that this rarefying change is followed later by a hardening process.

True bony ankylosis is an almost unknown result of arthritis de-

formans. Not entirely unknown, for it has been met with in the vertebral column, where this change has been described by Bowlby; but in the joints of the limbs with their far greater mobility it never occurs. Neither is there any tendency to the production of fibrous adhesions, a process which is so conspicuous in some forms of articular disease, and even in the arthritis of bleeders, which presents in other respects changes closely resembling those of arthritis deformans.

The changes in the shafts of the long bones are far less conspicuous than those of the articular portions, but, as Adams long ago pointed out, these portions also may exhibit an increase of size and of density.

Like the cartilages and bones, the synovial membranes are the seats of conspicuous morbid changes in arthritis deformans. In some cases in which operations have been performed upon joints thus diseased during the life of the patient, brilliant injection of the synovial membrane has been observed; but the most typical changes are the conspicuous thickening of the membrane, and the hypertrophy of the synovial fringes. Such hypertrophied fringes are conspicuous in all museum specimens of this disease. In the hypertrophied tufts fatty changes frequently take place, or they may become converted into cartilaginous masses which remain attached to the surface of the membrane by slender pedicles. These pedicles are very apt to be ruptured, with the result that the pellets of cartilage become converted into loose bodies lying free in the articular cavity.

Similar cartilaginous masses may also be present in the bursæ in the neighborhood of the diseased joint, and are easily and frequently to be detected by palpation in the bursa over the olecranon. It is not easy to understand how the opinion originated that one of the characteristics of arthritis deformans is the absence of any tendency to the accumulation of fluid in the cavities of the affected joints; yet it has frequently been asserted that this is the case, and one of the names assigned to the disease, viz., *arthrite sèche*, was intended to emphasize this view. So far as my own experience goes, and I could support my opinion by quotations from many eminent authorities who have devoted attention to the subject, this statement is quite opposed to the facts, and effusion, often of considerable amount, is frequently present both in the cavities of the joints and in the bursæ in their immediate neighborhood, many of which are doubtless in direct communication with the articular cavities. We possess an analysis of the articular fluid from a case of arthritis deformans by no less an authority than Hoppe-Seyler,[33] which gives the following result:

Mucin	28.19	parts per	1,000.
Albuminous substances	20.92	"	1,000.
Ethereal extract	0.93	"	1,000.
Alcoholic extract	1.30	"	1,000.
Watery extract	0.65	"	1,000.
Acetic extract	1.53	"	1,000.
Inorganic substances	8.79	"	1,000.
The total solids amounted to	57.28	"	1,000.
Water	942.72	"	1,000.
	1,000.00		

In the ethereal extract cholesterin, lecithin, and traces of fat were detected.

Next to the joint lesions the atrophy of muscles constitutes the most conspicuous change present in arthritis deformans. Post mortem the affected muscles are obviously wasted and have a brownish tint which is compared by Debove to that of dead leaves. Debove has further shown that the atrophy is of the type met with as the result of nervous lesions, the degeneration of the various component fibres being conspicuously unequal in its degree. Changes of the nature of neuritis have been detected by Pitres and Vaillard[36] in several cases of this disease which they have examined, and the amount of change which the nerves had undergone appeared to stand in a direct relation to the degree of atrophy of the muscles supplied by them.

Clinical Varieties.

It has already been mentioned in a previous section that the morbid changes in the joint structures which have just been described are met with in cases which differ widely among themselves in their clinical features. In one instance a woman, perhaps not more than thirty years of age, notices an enlargement and pain on movement of the joints of her fingers, and the disease, preserving more or less of a symmetrical distribution, spreads rapidly from joint to joint, until hardly an articulation in her body escapes its invasion; the disease showing no tendency to leave those joints which were earlier attacked as fresh ones become involved. In another instance an elderly man who has perhaps sustained a slight injury in the neighborhood of one of his hips suffers from pain in the hip-joint with limitation of its movement, without any involvement of other articulations. As the disease slowly progresses considerable shortening of the limb may result and the neighboring muscles will waste, but beyond the pain and the lameness which the disease produces he may suffer but little in his general health. In both the supposed cases the lesions in the joints

are of similar nature and both must be looked upon as examples of arthritis deformans. It is therefore necessary for purposes of clinical description to classify the cases and to discuss separately the etiology and symptoms of the several varieties of the disease.

The first and most important group embraces those cases which are characterized by the affection of many joints and which may be classed together under the name of multiple arthritis deformans. This is the condition which is unfortunately so common in women of all ages and of all stations of life, but which is especially frequent about middle life; which tends especially to invade the smaller rather than the large joints, producing, in many instances, conspicuous deformities of the hands and feet.

As a subvariety of this form may be grouped those cases in which the terminal joints of the fingers are alone affected by the disease in its most chronic form, displaying the small nodular outgrowths which are called, after the physician who first described them, Heberden's nodes.

As a second subvariety may be described a group of cases in which the lesions characteristic of arthritis deformans are developed as sequelæ of other joint affections, such as the arthritis of acute rheumatism, of gout, or of gonorrhœa. Such secondary cases, although they are much less common than the primary ones, must be reckoned with in an attempt to explain the pathology of the disease.

The second main group embraces those cases in which one or two joints, usually of the larger kind, are alone attacked, as in the second of the supposed cases above described. Indeed the typical example of this condition is the malum coxæ senile, the very chronic disease of the hip-joint which is not infrequently met with in elderly men.

If we adopt, as has here been done, the view that the changes in the joint structures afford the sole test of the nature of the case, and that where a certain set of morbid changes are met with there we have an example of arthritis deformans, it becomes logically necessary to include in a third main group a class of cases to which the name arthritis deformans is not usually assigned, namely, those in which, in the course of an organic disease of the great nerve centres, joint lesions closely resembling those of primary arthritis deformans are developed. Such lesions are by no means confined to locomotor ataxia, although the arthritis of that disease is the most familiar example and that to which the greatest amount of study has been devoted.

Following the classification above laid down, I propose to consider first and separately the etiology and clinical features of the primary

multiple cases which constitute at the same time by far the most numerous class, and that in which the disastrous effects of the malady are most conspicuous.

Multiple Arthritis Deformans.

Etiology.

It seems tolerably certain that hereditary tendency plays a far less conspicuous part in the causation of arthritis deformans than it does in connection with either gout or rheumatism. How great its influence is it is extremely difficult to ascertain with any approach to accuracy.

Even under the most favorable circumstances statistics of heredity have only a doubtful value unless they are the outcome of personal observations by medical men of the diseases met with in several generations of a family. When, as is so often the case, they are merely based upon the information supplied by individuals who are not in a position to give any accurate account of the nature of the maladies from which their parents or grandparents suffered, and whose acquaintance with their own medical histories is so imperfect as that possessed by the majority of the class from which hospital patients are drawn, their scientific value is reduced almost to the vanishing point.

This is true even of those diseases which have well-defined positions in the popular nosology, and, *a fortiori*, when we have to do with a disease such as that under discussion, which has no place at all in the popular mind as distinguished from rheumatism and gout, the difficulty of obtaining any trustworthy information will be greatly increased, or indeed practically insuperable.

The use of the term rheumatic gout affords an excellent example of the difficulties which surround investigations of this kind. In England arthritis deformans is the disease to which this name is commonly applied, and its employment in this sense has met with the approval of such high authorities as Dr. Fuller and Mr. Jonathan Hutchinson. When, on the other hand, we turn to the lower orders we find that among hospital patients rheumatic gout is the name by which true articular gout is almost invariably known, while arthritis deformans is included among the conditions which are described as "rheumatics." Obviously we have here a fruitful source of confusion and mystification.

Such statistics as I shall quote are based upon a series of five hundred cases which I extracted some years ago from my father's case books, and which were analyzed in a paper published in the

Transactions of the Royal Medical and Chirurgical Society in 1887.[37] These patients were drawn from the more educated classes of the community, and the statistics are therefore somewhat more trustworthy than if they had been based upon a similar series of hospital cases. The following table embodies the results arrived at:

Family history of gout	64
" " doubtful gout	10
" " rheumatism	48
" " rheumatoid arthritis	11
" " hand-joint affection	14
" " joint affection	24
" " rheumatic gout	1
" " deformed joints	1
" " crippling by rheumatism	11
" " sciatica	2
" " gout and rheumatism	7
" " " hand affection	5
" " " crippling	2
" " " joint affection	1
" " " deformed joints	6
" " gout, rheumatism, and rheumatoid arthritis	1
" " rheumatism and joint affection	4
" " " sciatica	1
" " " crippling	1
" " " rheumatoid arthritis	1
" " " hand affection	1
	216

In 284 cases there was no family history of articular disease.

It will be noticed that gout holds a prominent place in the list, being in the families of nearly one-third of all the cases.

Rheumatism occurs sixty-four times in all, but it is probable that some cases of arthritis deformans were so described. Of the remaining conditions such as hand-joint affection, deformed joints, and so on, which were probably of the nature of arthritis deformans, there are eighty-four examples.

The proportion of gouty family histories is certainly high and seems to lend support to the view expressed by some eminent authorities that the daughters of gouty fathers show a special liability to arthritis deformans. On the other hand it must be remembered that gout is extremely common in England among the classes to which these patients belonged.

The number of cases in which there was stated to be a family history of rheumatism was smaller, and there is little doubt that other conditions than true acute and subacute rheumatism were included under this head. In spite of this the proportion of such

histories is smaller than was the case among a series of five hundred hospital out-patients who had not themselves suffered from rheumatism, and who were only questioned as regards the occurrence of actual rheumatic fever among their nearest relations. This result is interesting from its bearing upon the pathology of arthritis deformans, in view of the opinion that it is merely a variety of chronic rheumatism.

When we turn from statistics to evidence of a safer kind there can be no question that not infrequently several cases of arthritis deformans occur in the same family, and although this is a less common occurrence than with gout and rheumatism, such examples are sufficiently common to warrant the conclusion that arthritis deformans is to some extent an hereditary disease. Even here we may be deceived and ascribe to the influence of heredity an association which is in reality due to several members of a family being alike exposed to the exciting causes of the malady.

As a typical example of such a family history I may quote the case of a poor woman who was under my care, who was a sufferer from typical arthritis deformans, and who stated her father and mother both had enlarged joints. She was one of fifteen children, only six of whom lived to grow up, and her three brothers and two sisters were all said to suffer from enlargement of the joints such as she herself exhibited.

I have not found that such family histories are to be obtained more frequently in cases in which the disease is developed at an unusually early period of life than in those in which it has a later onset; whereas those who suffer from gout at an early age nearly always have a strong hereditary tendency to that malady.

Such statistics as those above quoted appear to lend countenance to the idea which was formerly very prevalent that there exists an arthritic diathesis, a predisposition to articular disease, upon which gout, rheumatism, or arthritis deformans is apt to become developed. It is difficult to reconcile such a view with the fact that gout and rheumatism, at any rate, are not merely diseases of the joints with visceral complications, but are systemic disorders of which arthritis is merely a prominent manifestation. Nevertheless it must be confessed that the intricate way in which these various disorders are mixed up in certain families, and even occur in succession in the same individual, lends some countenance to the hypothesis of "arthritism."

Another group of observers[38] insist that the tubercular diathesis is one of the most important of the conditions predisposing to arthritis deformans, and maintain that a tubercular family history is extremely common among those who suffer from it. I believe that Dr. Fuller

was the first to advance this view. Tubercle contributes so largely to the general death-rate of the community that families in which that disease cannot be traced are perhaps rather in the minority, and in order to obtain any at all trustworthy statistical evidence upon this point, it would be necessary to compare the family histories of a series of patients with arthritis deformans with those of a series of patients not so afflicted. Such evidence would have more value than in the case of many other diseases, seeing that a death from consumption in the family makes a deep impression, and the information afforded on the point is as a rule fairly reliable.

I cannot say that I have ever been struck by any special liability of members of tubercular families to arthritis deformans, nor am I prepared to go with those who assign to the tubercular diathesis any very large share in its causation.

The Influence of Sex.—In the multiple form of arthritis deformans the influence of sex is strongly marked. Whereas gout is far commoner in men than in women and acute rheumatism falls with an approach to equality upon both, this disease attacks women far more commonly than men. Among the five hundred patients referred to above, there were no less than four hundred and eleven women and only eighty-nine men, and the inequality would have been still more conspicuous but for the fact that cases of the localized type were included as well as those in which many joints were involved; such examples constituted a considerable proportion of the male cases. This greater liability of the female sex is not confined to any particular period of life, but is observed even in the rare cases in which the disease occurs in children. It is least conspicuous in old age.

Influence of Age.—The liability is greatest between the ages of forty and fifty-five, but no age enjoys immunity from attack. Cases occurring in early adult life are apt to assume a more acute form, and the disease usually spreads then with much greater rapidity, than in older patients in whom it tends to advance but slowly and *pari passu* with other senile changes. The curve and table which are here appended show the ages of incidence in the five hundred cases.

Age at Commencement.	Females.	Males.	Age at Commencement.	Females.	Males.
0– 9	3	0	50–54	51	12
10–19	18	4	55–59	37	10
20–24	21	3	60–64	29	10
25–29	33	7	65–69	23	10
30–34	33	10	70–79	2	3
35–39	37	5	80–90	1	0
40–44	51	5	Doubtful	15	2
45–49	57	8			

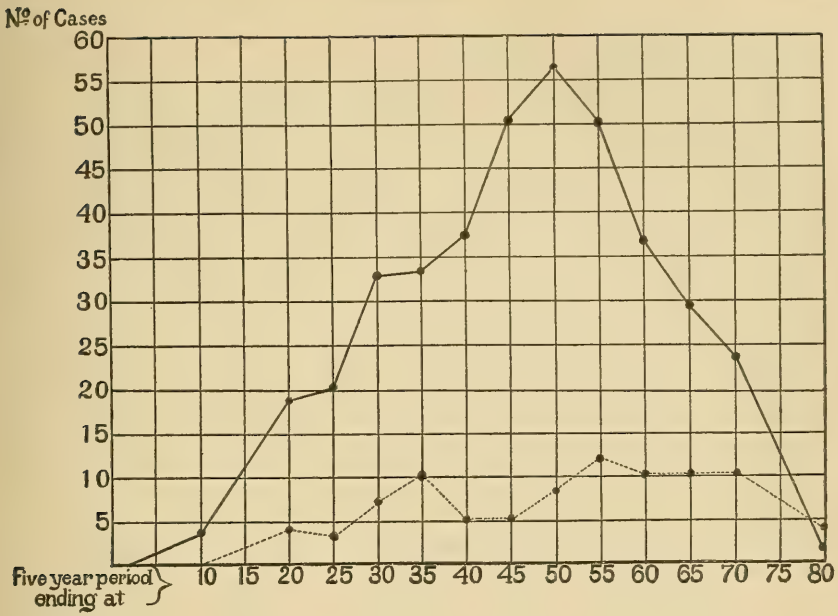

FIG. 1.

It will be noticed that in the curve of female cases (indicated by the continuous line) there is an unbroken rise until the five-year period 45–49 is reached, and from that period onward an unbroken fall. When on the other hand we turn to the male cases we find no such regularity of the curve (denoted by the dotted line) and no definite maximum. No doubt the falling off in the number of the female cases in later life is in part due to the smaller number of persons living; but this will not, I think, explain everything.

Influence of the Menopause.—The period of maximum liability in women is seen to correspond approximately to the years following the period of the menopause, and common experience confirms the teaching of the statistics upon this point, for it is found that many cases originate within a few years of that period.

Eighteen patients of the series dated the onset of the disease from a period within two years before the menopause, and no less a number than 41 from the two years following that event. In 5 cases the onset was dated from the actual menopause. Adding these together we find that out of the 411 female patients, no less than 64 dated the commencement of the malady from within two years of the climacteric.

Even in cases which date the onset from an earlier period of life the influence of the menopause is often conspicuous, for the disease is apt to acquire fresh vigor at that period, and to prove even more refractory to treatment than usual.

Exciting Causes.

Exposure.—There is a prevalent impression that exposure to cold and damp is among the most important of the exciting causes of multiple arthritis deformans, but I believe that the influence of these factors has been considerably exaggerated. Unquestionably those who suffer from it are extremely sensitive to changes in the weather, a fall of temperature or a spell of wet being frequently attended by a marked exacerbation of the articular pains, but even the patients themselves do not very often ascribe the commencement of their sufferings to such causes, or at any rate not so often as might be expected if they were very potent etiological factors. In this respect arthritis deformans stands in conspicuous contrast to true rheumatism, for an attack of the latter disease is perhaps more often than not ascribed to getting wet through, sitting in damp clothes, sleeping in a damp bed, or such like causes.

There is a tendency at the present day to discredit the influence of cold and damp as provoking causes of many diseases in which their influence was formerly unquestioned, such as pneumonia, acute nephritis, and other maladies; but however difficult it may be to reconcile their action with the teaching of modern pathology, the fact remains that the diseases in question frequently follow closely upon a definite exposure or chill, and it seems more scientific to attempt to adapt our theories to facts that rest upon such abundant evidence, than to reject observations which do not at first sight fit in with our theories.

Although it is not improbable that in the case of arthritis deformans the confusion of this malady with true rheumatism is largely responsible for the widespread opinion that it often dates from exposure, it is impossible to deny that in some cases these factors do really seem to play the chief part in this causation, and when this is the case the exposure has generally been prolonged. Living in a damp house or in a cold and damp neighborhood appear to be more potent than any sudden chill.

In only nine out of the five hundred cases was there a clear history of such an origin.

Dietetic Errors.—Dietetic causes do not appear to have any important share in the causation of arthritis deformans, that is to say, those which tend to excess; but scanty food or such as is not readily assimilated, by leading to malnutrition, certainly favors the development of the disease. In this respect the disease in question stands in conspicuous contrast to gout, and a dietary which would be suited to a gouty patient may prove, and often has proved, very detrimental to one suffering from arthritis deformans.

Indeed any condition which tends to lower vitality appears to have a decided influence in favoring the development of the arthritis, and of the few children who suffer from it a considerable proportion come from very poor homes.

Acute illnesses of various kinds must be included among the exciting causes and especially such as are apt to leave behind them a lasting impairment of the general health. Influenza possesses this quality in an eminent degree, and no one who has paid attention to the subject can fail to have been struck by the frequency with which patients who have developed arthritis deformans during the past few years date the commencement of their troubles from an attack of influenza acquired during the recent epidemic outbreaks of that malady. At the same time we must not forget that, owing to the enormous prevalence of influenza during those epidemics, the relation may be more apparent than real, and there is moreover a widespread tendency to ascribe almost all ailments to that cause. Of the occurrence of arthritis deformans as a sequel of acute rheumatism, as well of other diseases which tend to implicate the joints, I propose to speak at some length in a later section of this article.

Uterine Causes.—Some authors ascribe to uterine disorders a very prominent, if not the most prominent part in the causation of multiple arthritis deformans, and if their views are correct, an explanation is supplied of the excessive liability of the female sex. The influence of the menopause as a predisposing cause has already been discussed, and frequent and rapid child-bearing as well as excessive and prolonged lactation must be ranked among the conditions which cause exhaustion and so predispose to the disease. Of the 411 female cases of my series the condition of the menstrual function was noted in 176. In 105 cases the catamenia were regular and normal, and they were irregular in period or in amount in 71.

Two hundred and sixty-seven of the female patients were married and 144 were single.

The size of the family was noted in the case of 132 patients, and of these 92 had less than six children, and 40 had more; 2 had had thirteen, 1 fifteen, and 1 seventeen children.

In 5 cases the onset of the disease was said to have occurred after a confinement, in 3 after a miscarriage, and in 3 during pregnancy. Five patients had suffered from uterine or ovarian tumors. Dr. Ord[39] states that of a series of thirty-eight patients under his care no less than thirty had some uterine derangement or disease, either slight or severe, and he has observed that in some cases the menstrual periods are attended with an increase of the pain in the joints. In some cases pregnancy seems to hasten the progress of

the disease, but occasionally the patients suffer less at such periods than at other times.

Worry and Care.—Among the most interesting of the exciting causes of arthritis deformans are certain which can only be supposed to act through the nervous system, and which may be roughly classed as worry and care. The potency of such causes has been asserted by a number of observers, and histories of this kind are far too frequently volunteered by the patients to allow of any serious doubt upon the subject.

In the series of 500 cases there were 34 in which such causes were mentioned, and among such were included sudden losses by bank failures and sick nursing of near friends.

Nor are the pernicious effects of worry and care confined to the original causation of the disease, for such influences further tend to increase the patients' sufferings when the disease is already established, and the statement is not infrequently volunteered by them that any depression of spirits or anxiety always tends to make the pains worse.

Some cases have been recorded in which a violent mental shock or fright instead of prolonged worry has preceded the onset. Two cases are mentioned by Kohts[40] in which arthritis deformans followed the shock of a shell bursting close to the patient, and Leyden[41] states that in Strasburg many cases date their origin from the bombardment of that city during the Franco-German war. Here, however, the other conditions prevailing in a besieged city may have been partly responsible.

Injury.—The influence of injuries is more marked in the causation of the localized than of the multiple variety of the disease. Nevertheless cases are occasionally met with in which the characteristic changes have been developed in a single joint which has been the seat of an injury, and have afterward extended to other articulations. I have myself met with several cases in which this was stated to have been the course of events.

Lastly there remains a considerable proportion of cases in which none of the exciting causes mentioned above appears to have been at work, nor indeed can any definite cause for the onset of the disease be traced.

Clinical Features.

Condition of the Joints and Muscles.

Cases of multiple arthritis deformans fall into three main classes which may be described respectively as acute, subacute, and chronic.

In the acute cases, which are more commonly met with in younger

patients, the disease may easily be mistaken for acute rheumatism at its onset, and the diagnosis is rendered the more difficult by the fact that the pain may be altogether out of proportion to any obvious enlargement of the joints.

Such examples are rare in comparison with those of a more subacute type in which the enlargement of the joints is noticeable from the outset and the pain is severe, but seldom sufficiently so to confine the patient to bed. It is in women, usually under forty years of age, that this condition is most typically seen.

In the cases of the third or chronic class, commonly met with in persons advanced in life, the course of the disease is very slow, so that it will take many years to produce the amount of crippling that is developed in the course of a few months in the more acute cases.

Moreover the pain is, as a rule, far less severe and sometimes is quite insignificant, although the deformities may be very conspicuous.

Distribution of the Joint Lesions.—In the examples belonging to all the above types the distribution of the articular lesions tends to be very uniform. It is one of the peculiar features of arthritis deformans, in which it differs from other articular diseases, that the small joints of the fingers and toes are especially liable to be attacked even in the earliest stages of the disease.

It is true that the joint which is particularly liable to gout is a small peripheral joint, but as gout extends it tends rather to attack the larger articulations such as the knees, wrists, and elbows, and, as a rule, involves the finger-joints only in its later stages.

The most striking feature in the distribution of the lesions of arthritis deformans is the remarkable symmetry which they so often present. We frequently see the corresponding joints of the two hands picked out by the disease, and the invasion of one of the larger joints is, as a rule, quickly followed by the implication of its fellow. Sometimes a pair of joints little prone to other forms of arthritis, such as the carpo-metacarpal joints of the thumbs, are alone involved for a time.

This tendency to symmetrical distribution of the lesions, although so strikingly manifested in arthritis deformans, is not by any means confined to this form of articular disease. In acute rheumatism the joint lesions show hardly any symmetry of arrangement, it is true, but the distribution of the subcutaneous nodules of rheumatic children may be quite as symmetrical as that of the joint lesions of arthritis deformans. In gout, again, although unilateral distribution is the rule, we not infrequently see an attack in one great toe, closely followed by one in the corresponding joint of the opposite foot; but

here the peculiar circumstances of the first metatarso-phalangeal joint may be responsible for the occurrence.

Again to quote an affection not strictly articular, the syphilitic epiphysitis of infants is sometimes remarkably symmetrical. We must, therefore, be careful lest we find ourselves attaching undue weight to symmetrical distribution of lesions, as evidence of the nervous origin of those lesions.

Even in multiple arthritis deformans, symmetry is by no means the universal rule, and cases might be quoted in which the disease was strictly limited to the joints of one side of the body; as, for example, in a female patient whose right knee, elbow, and temporo-maxillary joints were alone affected.

As Charcot pointed out, the special liability of the small joints of the hands and feet to be attacked early is in part due to their peripheral situation, the disease showing a tendency to progress centripetally. In some individual cases this tendency is very marked, as, for example, in the case of a woman, aged forty-six years, whose feet were first attacked and afterward the jaw-joints, ankles, knees, hands, wrists, elbows, shoulders, and hips, in the above order.

If a table be constructed, based upon a large number of cases in all stages of the disease, showing the frequency with which the several joints suffer, it is obvious that those joints which tend to be earliest attacked will show the highest figures, and the order of frequency of implication will correspond roughly to the order of invasion.

Such a table was constructed for the five hundred cases which have already been frequently referred to, and this table is here reproduced. It will be seen that the peripheral joints tend to suffer most, and the hip-joints least; but the knees which are so liable to all kinds of arthritis, stand second upon the list, immediately after the hands.

Joints affected.	Total number of cases.	Percentage of total.	Joints affected.	Total number of cases.	Percentage of total.
Hands	430 in 500	86.0	Hips	73 in 500	14.6
Knees	303 "	60.6			
Feet	172 "	34.4	Temporo-maxillary	125 "	25.0
Ankles	137 "	27.4	Cervical spine	178 "	35.6
Wrists	133 "	26.6	Dorsal spine	15 "	3.0
Shoulders	125 "	25.0	Sterno-clavicular	2 "	0.4
Elbows	125 "	25.0			

It is a remarkable fact that the results were very similar in each hundred cases taken separately, especially as regards the liability of the hands and knees.

	I.	II.	III.	IV.	V.
Hands	86	85	85	86	88
Knees	68	65	59	55	68

In 252, or rather more than half the cases, the hand-joints were first affected; in 64 cases the knees, and in only 28 the feet, were first attacked.

The number of cases in the above table in which there was slight or severe affection of the temporo-maxillary and spinal joints will at once attract attention; and their liability is a characteristic feature of arthritis deformans, which sometimes lends valuable aid in the diagnosis of a doubtful case, for with the exception of gonorrhœal rheumatism there is no disease liable to be confused with arthritis deformans in which these joints are apt to be involved.

Clinical Character of the Articular Lesions.—Enlargement of the affected joints is the most important sign of arthritis deformans, and it is of three different kinds.

1. In the most chronic cases the enlargement is almost entirely due to osteophytic outgrowths upon, and lipping of the articular ends of, the bones. The shape of the enlarged bones is easily made out by the touch, and the osteophytes form distinct bony excrescences which are sometimes so sharp that they even threaten to pierce the skin. Lipping is particularly well made out at the lower end of the femur, and around the patella. This type of enlargement, which is very well seen in the hands of many old women, in whom the disease is almost of the nature of a senile change, is characterized by the abrupt increase of size at the level of the affected joint.

2. Fusiform enlargement to which the thickening of the synovial membrane and of the structures around the joint contribute largely. In this condition, which is seen in its most typical form in younger subjects, the transition from the normal to the swollen parts is much more gradual, as the name by which I have described it implies, and the osteophytic outgrowths are much less conspicuous.

This form of enlargement is perhaps best seen in the middle joints of the fingers and in the wrist. In the case of the latter the natural narrowing of the limb at the wrist may be entirely or almost entirely abolished.

3. The third form of enlargement is due to the accumulation of fluid in the cavity of the joint or in the neighboring bursæ. The enlarged bursæ are best seen upon the dorsal aspect of the wrist-joint, where they occasionally attain to a considerable size.

Enlargements of the second and third of the above classes are somewhat amenable to treatment, and the improvement in the appearance of a joint, when the bursal swellings disappear, and when the natural contour of the part is to some extent restored, is sometimes very striking. Osteophytic enlargement, on the other hand, is of course not amenable to treatment.

In the case of the terminal joints of the fingers, the enlargement of the ends of the bones is apt to produce a permanent and irreducible lateral deflexion of the terminal phalanges, usually toward the radial side, which is rendered more conspicuous by the ulnar deflexion of the fingers as a whole, with which it is often associated but which is a deformity of an entirely different type.

In the larger joints such as the knee or elbow, great swelling is often present, especially if there is fluid effusion, but even the swelling of the soft parts alone may be so considerable as to lead to the suspicion that fluid is present when it is not, until an examination is made.

In the earlier stages of the disease there is usually well-marked crackling in the joint on movement, such as is present in other forms of chronic arthritis, but when the bones have become bare of cartilage the grating of the bony surfaces upon each other, to which the grooves seen upon their surfaces post mortem bear eloquent testimony, may often be clearly felt.

Auscultation of the diseased joints, which I have frequently practised, has not afforded evidence of the condition of the parts in any way superior to that obtained by palpation.

Impaired mobility of the parts is naturally a prominent feature of the disease, and may be extreme when the bone changes are advanced, but actual bony ankylosis never takes place except in the joints of the spinal column, and there is no tendency to the formation of fibrous adhesions which contribute so largely to the immobility caused by other forms of chronic joint disease.

In advanced cases and even in the earlier stage of the disease the movements may be seriously impaired by spasm of the muscles. This is best seen in connection with the temporo-maxillary joint, which is often involved at quite an early period in the course of the disease, the affection usually showing itself as a temporary stiffness of the jaw at first. In many instances no more serious effects are observed, but occasionally the lower jaw becomes permanently fixed so that the patient has to be fed through gaps in the teeth. Specimens will be found in museums in which the condyle and its cavity are surrounded by extensive osteophytic outgrowths which must have most seriously interfered with movement at the joint, but even in severe cases the jaws of a patient which cannot ordinarily be separated to a sufficient extent to admit of the introduction of solid food, may be found to be separable to a much greater extent when the patient is put under an anæsthetic; showing how large a share muscular spasm has had in limiting the movements.

The same thing is noticed in the minor degrees of spinal affection

which often manifests itself at first as stiffness of the neck or back. The movements of the spine are often interfered with to a greater extent than the joint disease will explain, and the stiffness may be at first temporary and pass off. Moreover when the cervical spine is affected the head is often drawn to one side. But spondylitis of this kind may assume far more severe forms, and considerable osteophytic outgrowths may be produced around the spinal joints; or, as has been said, actual bony ankylosis may take place. As in other diseases of the spinal column, radiating pains and causalgia may bear witness to the implication of the emerging nerve roots by the morbid process.

Muscular Atrophy.—After the joint lesions and deformities, muscular atrophy is perhaps the most conspicuous of the phenomena of arthritis deformans.

By some this atrophy is regarded as merely an example of that which is apt to affect the muscles in the neighborhood of joints which are the seat of any form of chronic and even of acute arthritis, and it is quite certain that the disease under consideration must, like other forms of arthritis, be attended by such wasting, so that, in part at least, the changes in the muscles must be of this secondary nature. There are, however, those who believe that there are other influences at work in its production, and that the joint lesions and wasting may be looked upon as parallel manifestations of the same morbid process, due to a common cause and advancing *pari passu*.

The so-called arthritic muscular atrophy is a phenomenon of much interest, and one which cannot be explained as merely an effect of disuse, as has been clearly shown by Charcot and others. In cases in which the patient is confined to bed by an affection of one hip or knee joint, both lower extremities are kept at rest, but the wasting of the muscles of the diseased limb altogether exceeds that on the sound side, and moreover the atrophy of the thigh muscles is accompanied by an exaggeration of the knee jerk.

Raymond[12] arrived at the following conclusions as the outcome of an experimental study of the muscular atrophy following traumatic joint lesions in animals:

1. That the limb the joint of which is injured exhibits various symptoms, such as functional impotence, increased reflexes, idio-muscular contractions, and muscular atrophy.

2. That such atrophy is not produced when the posterior nerve roots corresponding to the limb are divided. Hemisection of the cord hastens the atrophy of the muscles of the corresponding limb, but does not affect that of the opposite limb when the joints of both are injured.

3. The muscular atrophy which follows joint lesions is of reflex

origin, and is due to purely dynamic alterations in the cord, since no anatomical lesion of the anterior cornua or peripheral nerves is found.

These results support the views advanced by Paget, Charcot, and others as to the reflex nature of the changes, and Gowers[43] regards such a theory as the only tenable one. He adds: "It is, however, an interesting fact that the wasting is accompanied by an increase in the myotatic irritability. We have in fact the condition that often results from slight degeneration of the pyramidal tracts, and must be immediately due to the changes in the terminations of the pyramidal fibres in the gray matter—increased myotatic irritability and slight wasting, and merely a slight diminution in the electrical irritability, similar to each current."

The atrophy of arthritis deformans resembles that connected with other joint affections in tending to affect the extensors more than the flexors, although both sets of muscles may share in the atrophy, but in some cases the wasting is extreme and some of the affected muscles occasionally yield even the complete reaction of degeneration.

These facts are among those relied upon by authors who maintain the primary nature of the muscular atrophy in this disease, and who further maintain that the atrophy may have a wider distribution than the joint lesions, affecting limbs or portions of limbs in which the joints are as yet intact.

It is possible and indeed probable that in arthritis deformans we have superadded to the reflex atrophy a primary muscular affection similar to the dystrophy of the skin which is not infrequently observed, but this would not account for the whole of the atrophy, since we cannot suppose that such a joint disease as arthritis deformans will not share with all other joint diseases the tendency to produce a reflex atrophy. It is certainly the rule that the atrophy follows rather than precedes the joint lesions, but it is an interesting fact which perhaps lends support to the idea of a mixed atrophy, that although increase of myotatic irritability is often observed, it is by no means constant in limbs affected by arthritis deformans, even when its absence cannot be explained by the condition of the joints.

Sometimes the stiffness or painful condition of the joints prevents the examination of the reflexes, but this is not often the case.

Some years ago I examined the condition of the supinator, triceps, and knee jerks in fifty patients suffering from arthritis deformans, and the results may be summed up as follows:

Among 23 cases which exhibited well-marked muscular atrophy, there were 18 in which increase of some of the reflexes was observed; whereas in 27 cases in which the atrophy was comparatively slight there was increase of reflexes in 14 only.

As in other varieties of arthritic muscular atrophy the increase of myotatic irritability is not always confined to the affected limb. In cases in which one hip-joint is alone affected both knee jerks may be increased. In some cases the increase is very conspicuous. Thus a man aged thirty-two years had all the reflexes greatly exaggerated. His hands, feet, elbows, knees, shoulders, and ankles were all the seats of arthritis deformans of a severe type. A tap upon either supinator tendon caused contraction of the triceps and some clonic spasm, and when the triceps tendon was struck clonus was again produced and contractions of all the arm and scapular muscles. There was also conspicuous exaggeration of the knee jerks, with slight foot clonus on the left side. The muscles exhibited conspicuous atrophy and the muscular deformities were considerable. A somewhat similar case, in which a tap upon the patella or triceps tendon not only produced a greatly exaggerated jerk, but also gave rise to contraction of the trunk muscles, has been recorded by Mader[11] of Vienna.

Occasionally mere extension of a limb serves to set up a clonic spasm.

Muscular Contracture as a Cause of Deformities.—Spasmodic contracture of the affected muscles plays a very important and conspicuous part in the production of the deformities met with in severe and long-standing cases of arthritis deformans.

In the limbs this cause may lead to flexion and almost complete deprivation of mobility, but it is in the hands and fingers that such effects are best seen and studied.

The muscular deformities are much more conspicuous than those due to bony enlargements, and are usually most extreme in cases in which the latter are least marked. In the hands they lead to distortions similar to those which result from chronic muscular spasm apart from any affection of the joints, as in old cases of infantile paralysis, and in cases in which there has been an antecedent hemiplegia followed by rigidity. In one respect, however, they differ from these, viz., in the almost constant presence of a marked deflexion of the fingers toward the ulnar side.

This ulnar deflexion is only met with after affections of the metacarpo-phalangeal joints, and I believe that the involvement of these joints at some period is a necessary factor in its causation. One sometimes sees this deformity in its most extreme form in patients who have suffered on one or more occasions from rheumatic fever affecting the hands, but in whom the knuckle-joints show no sign of disease other than the relaxation of their ligaments which dates from the antecedent inflammation.

In its earlier stages the production of the deflexion cannot cer-

tainly be due to the action of the extensor muscles, for the tendons will be found lying in their grooves and sharing in the bend at the knuckles. In extreme cases, on the other hand, the tendons may lie upon the ulnar side of the joints when the knuckles are flexed, but return to their proper positions when the fingers are extended. In health a certain degree of deflexion of the fingers to the ulnar side is readily produced, but any attempt to bring about a similar deflexion to the radial side fails, and it seems probable that in disease the greater amount of ulnar deflexion of which the relaxed ligaments allow is taken advantage of by the force of gravity, aided perhaps by wasting and consequent weakening of the abductor indicis.

Whether or no this be the correct explanation of the phenomenon, the fact remains that ulnar deflexion of the fingers is not a simple effect of muscular spasm, but implies present or antecedent disease of the metacarpo-phalangeal joints.

The deformities of the hands which are strictly due to muscular spasm have been elaborately classified by Charcot under two main classes, each with several subdivisions. The basis of the classification is the condition of the middle joints of the fingers, which are sometimes held flexed, while in other cases they are hyperextended. Permanent flexion of any of the finger-joints is apt to be compensated for by hyperextension of others, and in this way a variety of grotesque deformities are produced.

In Charcot's type of extension the terminal phalanges are flexed upon the second row at an obtuse or even at a right angle.

The second phalanges are hyperextended upon the first.

The first phalanges are flexed upon the metacarpal bones.

Subvarieties of this type are met with.

In the cases belonging to the type of flexion the terminals are extended upon the second phalanges, which are in turn flexed upon those of the first row. The first phalanges are extended upon the metacarpals; and the carpus is flexed upon the forearm. This type also admits of subvarieties. The interossei doubtless play an important part in the causation of these deformities, for they are specially apt to be affected, and if they preponderate over the other muscles they will produce flexion of the first phalanges upon the metacarpals, and the type of extension will result, whereas if they are weak there will be hyperextension at the same joints and the type of flexion will be produced.

Very rarely dropping of the wrist is met with, as distinguished from active flexion at that joint, and this, when present, is probably due to the affection of the peripheral nerves which has been found post mortem in cases of arthritis deformans by Pitres and Vaillard.

Abarticular Phenomena.

Cutaneous Pigmentation and Dystrophy.—Kent Spender,[15] of Bath, was the first to call attention to the frequent development of pigment spots upon the skin in the neighborhood of joints affected with arthritis deformans, and even goes so far as to say: "Concerning the disseminated form of pigmentation, commonly called freckles, I must express an opinion that there is no single point so diagnostic, so absolutely connotative of early osteo-arthritis. My observations lead to the belief that it exists in about two-thirds of the undoubted cases."

More recently the same point has been independently insisted upon by R. Wichmann,[16] of Brunswick, who was obviously unacquainted with Spender's observations.

If looked for, spots of pigmentation, frequently so dark as to appear almost black, will often be found in the neighborhood of the affected joints, and in a considerable number of cases their development has been apparently directly associated with that of the articular lesions; but such spots are often to be seen upon the skin of patients who are not suffering from arthritis deformans but who have reached the period of life at which that disease is most common; and even where the two are associated the patients will often state that the pigmentation has been there as long as they can remember. It is often very difficult to ascertain whether the pigmentation of the skin has any real connection with the joint troubles, and therefore, while fully admitting the accuracy and interest of Spender's observations, I am not prepared to attach to the pigment spots the same diagnostic importance that he does.

In a considerable proportion of cases some degree of glossiness of the skin is observed. Sometimes the skin in the neighborhood of the affected joints has merely an unusually shiny appearance and seems to be unduly thin; but occasionally the typical pink tint and glossy surface of cutaneous dystrophy is met with. The late Dr. Hadden[17] recorded an instance in which the changes had progressed a stage further, and trophic ulcers had developed.

Dystrophic changes may also be present in the nails, but usually the impairment of nutrition is slight and shows itself as a rule in the form of longitudinal striation such as is so commonly seen in gouty subjects. Œdema of the legs was observed by Charcot and Vidal, and such œdema is certainly sometimes developed in cases of arthritis deformans apart from any recognizable visceral lesions to which it can be ascribed. Local sweating has been observed by Spender, Wichmann, and others, but this phenomenon is not peculiar to arthritis deformans among diseases affecting the joints.

Subcutaneous Nodules.—The occasional development in apparently typical cases of arthritis deformans of subcutaneous nodules closely resembling both in their seat and characters those seen in children suffering from acute or subacute rheumatism, presents a problem which is not yet ripe for solution.

As long ago as 1883 Payne[48] called attention to the occurrence of subcutaneous nodules in cases of chronic rheumatoid arthritis, suggesting that they probably were only developed in the neighborhood of inflamed joints. A noteworthy example of the condition has been placed on record by Wallace Anderson.[49] They are also mentioned by Fagge Howard and some other authors. Some cases of this kind were lately recorded by Newton Pitt.[50]

The following case, which was under the care of Dr. Andrew in St. Bartholomew's Hospital, affords an excellent example of the condition:

E. C., male, aged 39, with no family history of joint disease, suffered fifteen years previously from a slight rheumatic attack. His present illness began with an attack of influenza five months before his admission. A fortnight later he had pain in the back, and articular pains which shifted rapidly from joint to joint, and was confined to bed for seven weeks. The pains had never ceased in the interval. The nodules were first noticed two or three weeks after the joints became affected, and had gone on forming ever since. When seen he had many nodules upon the scalp, forehead, elbows, palmaris and extensor tendons of the hands, knees, and in many other situations. He stated that some were decreasing in size. The finger-joints were considerably enlarged, and there was marked muscular atrophy as well as some ulnar deflexion of the fingers. The shoulders, wrists, hips, knees, and feet were also involved. He had suffered from some stiffness of the temporo-maxillary joints, and on the back of the hands were many small pigment spots which he said had appeared since the commencement of his illness. The nodules on the knees were well marked, but there was no bony enlargement. All the nodules were curiously tender and in this respect only differed from the ordinary rheumatic nodules. The heart's apex beat was outside the nipple line and the first sound was impure, but there was no distinct murmur. The patient stated that in the earlier part of his attack he had sweated profusely.

It is possible that the above case was originally one of rheumatism on the top of which arthritis deformans had developed, as sometimes happens, and that the two disorders were both present side by side; or possibly the disease was not true arthritis deformans but the condition simulating it which is sometimes met with as a sequel of rheumatism, although certain features of the case, such as the implication of the temporo-maxillary joints, are opposed to such a view of its nature.

A third possible explanation is that in the course of arthritis deformans nodules closely resembling true rheumatic nodules may be developed, the acceptance of which explanation would, it must be confessed, lend strong support to those who maintain the rheumatic nature of the malady.

It will be noticed that in this instance the nodules were tender, a very unusual feature in rheumatic cases, but which has been noticed by Newton Pitt in other similar cases; and that they appeared at a period of life in which the ordinary rheumatic nodules are extremely rare. These latter are indeed commonest in children and are seldom met with in patients who have passed twenty-five years of age.

Newton Pitt has found that the nodules last longer in cases of arthritis deformans than in rheumatic cases, sometimes persisting for many years, and are not associated with cardiac lesions. He further remarks that they may attain to an inch in diameter, and I also have seen examples of such large nodules. Sometimes what appear to be nodules upon the elbows are found on examination to be loose bodies in the bursa over the olecranon.

In one case which Pitt describes, there was extensive fibrous thickening of the affected parts rather than discrete nodules, and associated with this was a marked amount of peripheral asphyxia which he ascribes to the pressure of the growth.

A case in which extensive exudations similar to those more recently observed by Newton Pitt has been described by Middleton, of Glasgow.[51]

Pain in Arthritis Deformans.—The pains experienced by sufferers from arthritis deformans are of several different kinds, and may be classified as follows:

1. Articular pains, due to the morbid process in the joints;

2. Pains of a neuralgic type which are experienced in other situations than in the diseased joints;

3. Cramps, due to painful spasm of the muscles in the neighborhood of diseased joints;

4. Radiating pains due to involvement of nerve roots, met with only when the vertebral column is implicated.

1. The pain in the diseased joints varies very greatly in severity, and in some cases of the most chronic type it is so slight that the patients themselves lay but little stress upon it, being far more concerned at the disfigurement which the disease produces. On the other hand it is often very severe, and may cause intense suffering. Movement tends to increase the pain, and the patients frequently suffer more when warm in bed. As already mentioned, changes of weather, and even worry and anxiety are often the causes of exacer-

bation. The patients, as a rule, describe this pain as having a gnawing or burning character.

The joints are apt to be most painful at a comparatively early period of their implication by the disease; that is to say, at the time when the articular cartilages are undergoing destruction; as the disease progresses and the ends of the bones become bared and eburnated, the severity of the pain may be greatly diminished. Indeed one may usually give the patients the consolation of assuring them that even although the progress of the disease be not stayed by treatment, time will at least bring alleviation of suffering.

2. The neuralgic pains have been specially dwelt upon by Kent Spender, who calls attention to a neuralgic pain in the ball of the thumb or on the inner side of the wrist, which, like the pigment spots, he looks upon as an almost pathognomonic symptom in the early stages of arthritis deformans. To the same category may be referred the pains in the bones, which can readily be distinguished from the true articular pains.

3. Painful muscular cramps, although less common than the above, contribute materially to the sufferings of the patients. Like cramps from other causes, they are of sudden onset, and are apt to cease as suddenly as they commenced. They are met with in muscles in the neighborhood of the diseased joints, and the joints themselves are rendered more painful by the action of the muscles upon them. I believe that Charcot was the first to call attention to such cramps as a prominent feature in some cases of arthritis deformans.

Fortunately treatment is often very effectual in relieving and also in warding off such attacks.

4. If a careful analysis is made of the pains from which patients with arthritis deformans suffer, it will be found that radiating burning pains, following the course of a spinal nerve, and associated with spondylitis, are decidedly less uncommon than might be supposed. They occasionally follow the course of the occipital nerves, or take the form of brachialgia or intercostal neuralgia, and sometimes assume a very severe form.

Leyden[52] records the case of a man, aged sixty-four, who suffered from arthritis deformans, which, among other parts, involved the lumbar spine. One night the patient was suddenly attacked with intense pain in the left thigh, and on the following morning could not stand on account of it. The pain gradually passed off, leaving a sensation of deadness in the limb.

A middle-aged woman, at present under my care, who has multiple arthritis deformans, and pain and stiffness of the cervical and dorsal spine, complains of a pain extending down the left arm to the

fingers, which she describes as of a burning character "like mustard," and has also a sensation of numbness in the ring and little fingers of the left hand.

Minor Sensory Symptoms.—Numbness and tingling of the hands and feet are not at all uncommon symptoms, and may be met with very early in the disease, even before there is any recognizable affection of the joints of the part. I have seen many cases in which such symptoms were experienced, and Homolle[53] and Howard [54] have both called attention to their occurrence in the early stages of this malady.

Febrile Disturbance.—In chronic cases of arthritis deformans there is little or no febrile disturbance, but when the disease assumes its acute or subacute form the temperature may be considerably raised. In many cases the curve conforms to the hectic type, showing a normal temperature in the early part of the day, and a rise of two or three degrees toward evening. Sometimes, as Kahler [55] has pointed out, the variations in the amount of febrile disturbance appear to be independent of any changes in the condition of the joints.

Circulatory Disturbances.—One of the phenomena of arthritis deformans observed by Spender is the undue frequency of the pulse, which is a very frequent and early symptom, and which is quite independent of any rise of temperature. It is quite a common thing to meet with a pulse rate of over 100 beats in the minute, and sometimes, as Duckworth says, there is associated with this palpitation of the heart.

The tension of the pulse tends to be low rather than high as it is in gout.

The following table gives the rate of the pulse in 25 cases of multiple arthritis deformans, taken without any selection:

Sex.	Age.	Pulse rate.	Sex.	Age.	Pulse rate.
F.	65 years	112 per minute.	F.	48 years	104 per minute.
M.	50 "	92 "	F.	50 "	100 "
F.	65 "	72 "	F.	53 "	112 "
F.	52 "	100 "	M.	38 "	60 "
F.	30 "	80 "	F.	29 "	96 "
F.	40 "	104 "	F.	49 "	100 "
F.	54 "	80 "	F.	54 "	80 "
F.	40 "	72 "	F.	57 "	80 "
F.	48 "	90 "	F.	73 "	96 "
F.	60 "	84 "	F.	48 "	100 "
F.	36 "	88 "	F.	41 "	96 "
F.	60 "	120 "	F.	35 "	80 "
F.	43 "	120 "			

The Urine.—Little special study has been devoted to the urine of patients suffering from arthritis deformans, nor is it likely that such

a study will yield very important results. Albumin is not present unless there is intercurrent disease of the kidneys. A diminution of the earthy phosphates has been observed by Drachmann,[56] and Angel Money speaks of unusually wide variations in the amounts of urea and uric acid excreted.

Visceral Lesions.—One of the most characteristic features of arthritis deformans which lends powerful support to the view that its development is more probably dependent upon nervous influences than upon any systemic poison, is the absence of any visceral lesions which are developed with sufficient frequency in its course to be regarded as primary manifestations of the morbid process which produces the articular lesions.

I am aware that in making the above statement I am running counter to the views of observers whose opinions are entitled to the highest respect, such as Charcot, Besnier,[57] and Kahler,[58] but I believe that the statement will nevertheless be confirmed by the experience of most physicians who have been brought much into contact with the disease under discussion.

The supposed relationship of arthritis deformans with acute rheumatism has led to a careful search for cardiac lesions developed in its course, and the extremely limited amount of success which has attended upon this search appears to me only to emphasize the fact that cardiac lesions are not ordinary accompaniments of the malady.

I believe that I am justified in expressing the belief that valvular heart lesions are not more common among the subjects of arthritis deformans than among others who do not suffer from that malady, and I cannot recall a single instance in which there was satisfactory clinical evidence of the development of valvular lesion in its course which could not be equally ascribed to concomitant atheroma, or of pericarditis which could not be attributed to intercurrent renal disease.

Undoubtedly we meet with valvular lesions in patients with arthritis deformans which are apparently of rheumatic origin, but these can almost invariably be traced to antecedent attacks of true rheumatism. Even when this is not the case the origin of the heart trouble in a rheumatic attack cannot be excluded, for we know that in early life serious endocardial lesions may date from an attack of rheumatism in which the joints may entirely escape.

I might quote in support of the views here enunciated the statements of various authorities whose names may be set in the balance against those of observers who have maintained the contrary.

There is no more convincing evidence that the renal disease which sometimes complicates arthritis deformans, and is among the more

frequent causes of death among the patients, is anything more than an intercurrent disorder; and in this same category may be classed bronchitis and phthisis which also hold somewhat prominent places among the causes of death.

Affections of the organs of special sense are sometimes met with, and sclerotitis, iritis, and conjunctivitis have been described as complications; but it is a significant fact that Fuller, who at one time looked upon them as such, expressed, in the later editions of his work, the view that the cases upon which his opinion was based were really examples of gonorrhœal rheumatism, of which these affections of the eye are not uncommon manifestations.

Deafness may result from the invasion by the disease of the articulations of the small bones of the ear, and is then an actual manifestation of the disease.

There is certainly no form of skin disease which stands to arthritis deformans in any such relation as that in which eczema stands to gout.

General Condition of the Patients.

Any person who suffers from a chronic disease attended by almost constant pain, and which often renders exercise impossible, must necessarily deteriorate in general health, but in many cases of arthritis deformans this deterioration is often less than might be expected. Many patients in whom only a limited number of joints are affected, and who are able to get about, do not suffer materially in this respect, and, as Sydenham wrote long ago, retain an unimpaired appetite, while their bodily health does not materially suffer. This is especially the case with elderly people who suffer from the disease in its most chronic form, and of whom it may usually be said that their life is not in any way shortened thereby.

In more acute cases, however, the patients who are weakened by arthritis deformans readily fall victims to intercurrent disorders to which they are rendered especially liable, and occasionally they exhibit a most conspicuous degree of anæmia of a progressive type, the development of which is of very evil prognostic significance. A recent writer, Russell Fosbrook,[7] assigns to anæmia a very prominent place among the causes of the disease, and expresses the opinion that its onset is usually preceded by a condition of anæmia not usually recognized in the face or buccal mucous membrane, but almost always in the conjunctivæ. This anæmia is characterized by a simple deficiency both of red corpuscles and of hæmoglobin. The point is one upon which further observations are desirable.

Prognosis.

Seeing, then, that arthritis deformans has no tendency to attack any vital organ, it is no matter for surprise that the disease is apt to persist for many years, sometimes rendering the patient a helpless cripple, and being terminated only by the supervention of some intercurrent disorder, such as those alluded to above, or of others which are common in later life, such as cancer. The disease, if left to itself, tends to progress with greater or less rapidity, but its progress may be spontaneously arrested at any time. Under appropriate treatment such arrest or even marked improvement is not infrequently observed, but when the disease is well established and serious deformities have been produced, little can usually be done beyond relieving pain.

The prognosis is therefore better the earlier the patient comes under treatment.

The chances of improvement are greatest in the more acute cases, and in the younger subjects; while in the chronic form seen in elderly people there is the consolation of knowing that if there is less prospect of amelioration, the progress of the disease is much slower, and the chance of serious crippling is infinitely less.

A satisfactory prognosis can only be given after the case has been watched for a time, and the rate at which it tends to progress, the degree to which it responds to treatment, and the amount of its tendency to involve fresh joints has been noted. As regards the effect of treatment especially no notion can be formed from an initial examination of the patient. The prognosis as to life is favorable except when some intercurrent disease already exists, or when the patient exhibits a profound degree of anæmia; but unless there has been an opportunity of watching the patient, the prognosis of the joint affection should be given with great caution, while it should always be borne in mind that by discouraging the sufferer unduly, we tend to produce a mental depression which itself favors the further development of the disease.

Heberden's Nodes.

When speaking of the differences in the clinical features of the more acute and chronic forms of arthritis deformans I pointed out that in the more chronic cases, such as are best seen among aged folk, there is much less swelling around the affected joints, and the outlines of the articular ends of the bones, which are deformed by

lipping and by osteophytic outgrowths, can be made out and even seen with great distinctness.

There is a subvariety of the polyarthritic form of the disease in which such chronic enlargements are limited to the terminal interphalangeal joints, and the deformities so produced are universally described as Heberden's nodes, because it was Heberden who first described this condition. In his work published in 1805, which has been already referred to as containing one of the very earliest differentiations of arthritis deformans from rheumatism and gout, this author wrote as follows: "I have never rightly understood the nature of the tumors attaining to the size of a pea, which are sometimes developed near the third joints of the fingers. They have certainly nothing in common with arthritis (gout), since they are met with in many persons to whom that disease is unknown. They remain throughout life, are devoid of all pain, and show no tendency to ulceration. The deformity is more conspicuous than the inconvenience that they cause, although the movement of the fingers is somewhat impeded by them."

It is perfectly true that, as Heberden states, these nodes are often quite painless, and the patients are frequently more concerned by the disfigurement which they occasion than by any other trouble to which they give rise.

In many cases the development of Heberden's nodes appears to be nothing more than a senile change; and there is usually no tendency to further extension of the disease. Sometimes they are met with in association with the local form of arthritis deformans in the hip or shoulder joints.

The nodes have their origin in osteophytic outgrowths upon the articular ends of the bones, and the affected joints exhibit, as Charcot and others have shown, the ordinary changes which are produced by arthritis deformans. In the most typical cases two bony nodules are situated symmetrically upon the dorsal aspect of the terminal joint, one upon either side of the middle line, but where the morbid process is more active the swelling may be more uniform, and the entire joint may exhibit a fusiform enlargement.

Sometimes the nodes are greatly increased in size by small cystic swellings which may appear translucent when examined against the light, and which most probably consist of hernial bulgings of the synovial capsules of the joints. When the patients are led to puncture these cysts, a clear viscid fluid exudes.

In some instances there is a marked lateral deflexion of the terminal phalanges, and when this is the case the deflexion, unlike that of the fingers as a whole, is always toward the radial side.

The terminal joint of the thumb usually escapes even when all the fingers are affected.

The so frequent limitation of the disease to the terminal joints of the fingers may be regarded as a particular instance of a general law, to which, however, there are numerous exceptions, that arthritis deformans tends to begin peripherally.

Although seldom acutely painful these nodes may cause marked limitation of the movements of the affected joints, and thus greatly impair the utility of the hands for any delicate movements. Like the other forms of multiple arthritis deformans they are much more frequently seen in women than in men.

Charcot found that Heberden's nodes were in a considerable number of instances associated with malignant growths, especially of the uterus. Seeing that there is certainly a connection between the articular lesions and uterine disorders, it appears probable that malignant disease may have some share in their causation, but there is little evidence of any connection between the disease under discussion and cancer *qua* cancer, nor, as far as I am aware, has this point been dwelt upon by any other observer.

A far more complicated question is presented by the relationship of Heberden's nodes to gout. As we have seen, Heberden himself pronounced very emphatically, and probably too emphatically, against the existence of any such connection, but since his time a number of physicians, and among them Begbie, have maintained the opposite thesis. Sir Dyce Duckworth believes that in some instances the nodes are certainly of gouty origin, and Dr. Emil Pfeiffer,[59] of Wiesbaden, while admitting that they are to be found in many persons who have never suffered from actual articular gout, maintains that their presence always affords evidence of a gouty tendency, either inherited or acquired. This conclusion he bases upon the results of the application of his uric-acid filter test to the urine of the patients, a test the value of which for diagnostic purposes has been seriously questioned by Sir William Roberts and others.

Pfeiffer makes the further statement that in true arthritis deformans the terminal joints of the fingers always escape, a statement which is certainly at variance with common experience.

Dr. Kent Spender, of Bath,[60] strongly maintains the alternative view, and although I have certainly seen cases in which the development of Heberden's nodes has been associated with unquestionable evidences of a gouty tendency, I find it difficult to doubt that in the great majority of instances they are manifestations of an extremely chronic form of arthritis deformans.

They are perhaps most commonly met with in elderly women of

the lower orders, who have spent a long life in more or less strenuous manual labor, and it is not easy to imagine that in such cases there is constantly an underlying gouty tendency in view of the fact that the less questionable manifestations of that tendency are exceedingly uncommon among such patients.

Arthritis Deformans in Children.

The time is not yet ripe for any adequate description of arthritis deformans as it occurs in children, for the whole subject of the chronic joint diseases of children constitutes a chapter in clinical medicine which still remains to be written.

Unlike most of the other maladies which are especially common at the later periods of life, arthritis deformans, although rare, cannot be spoken of as extremely rare in the period of childhood, and is certainly more commonly met with in children than true gout. On the other hand I am convinced that some cases which, on account of their clinical features, are classed as examples of arthritis deformans in children are not truly of that nature, if it is permissible to adopt the presence of the changes in the cartilages and bones described above as the criterion; and this conviction is based upon post-mortem evidence.

How great is the difficulty of assigning to any definite category some at least of the chronic arthritides of children is well illustrated by some cases recorded by T. Barlow[61] and W. Pasteur.[62] In both instances chronic affection of many joints was accompanied by a peculiar hidebound condition, and in Barlow's case there were many subcutaneous nodules which both in their distribution and clinical characters resembled very closely the subcutaneous fibrous nodules of rheumatic children which are so closely associated with the name of that physician.

Cases somewhat similar have been described by Wagner,[63] of Munich.

In some cases the clinical features leave no doubt upon the mind that we are really dealing with the same disease from which adults suffer, but such examples are least uncommon in the later years of childhood.

The following will serve as an example:

Eliza C., aged 10 years, whose maternal grandmother had suffered from acute rheumatism, but in whose family there was no history of arthritis deformans or gout, had always been a delicate child, and her health had lately been further impaired by the privations which the family had undergone owing to her father being out of work. Two

months before she was first seen she began to complain of pain in the middle joint of the index finger of the right hand, and shortly afterward the corresponding joint of the right middle finger became involved.

She exhibited enlargement of the middle joint of the right middle, ring, and little fingers, and also the same joint of the left middle finger.

There was already some distortion of both hands conforming to the type of flexion of Charcot. The wrists were also involved, being somewhat painful and swollen. The muscles of the right arm were markedly atrophied. The supinator jerks were not obtained, the triceps jerks were normal, and the knee jerks were feeble. No numbness or tingling had been noticed.

The cervical spine and temporo-maxillary joints were not involved.

The pulse-rate was 104 per minute, and the beats were irregular.

Nothing abnormal was detected in the heart or lungs.

In this instance we have a delicate child, developing, after a period of scanty food and general privation, a condition indistinguishable from the arthritis deformans in adults; attacking first, as that disease does, the smaller peripheral joints and unattended by any recognizable cardiac lesion.

The subject of arthritis deformans in children has been specially studied by Moncorvo [64] in Brazil and by Diamantberger [65] in Paris, the latter of whom has devoted a lengthy monograph to its discussion. As the outcome of the personal study of some cases of the kind, and of the examination of recorded examples, Diamantberger concludes that the special liability of the female sex which is so conspicuous in adult life is also noticeable in childhood; that in some instances direct inheritance of the disease can be traced, but that bad hygiene, cold, privation, and some kinds of infection contribute to its development. He states that in most cases the disease tends to be somewhat acute, and that the prognosis is more favorable in childhood than in adult life.

Among clinically associated conditions Diamantberger mentions exophthalmic goitre, a point which has also been dwelt upon by Kent Spender, who adduces as points of affinity between these two maladies the occurrence in both of pigmentation of the skin, rapidity of the pulse, and tremor.

Secondary Arthritis Deformans.

It is often very difficult to be sure whether or no the chronic articular lesions which follow as the sequelæ of various acute forms of arthritis are actually of the nature of arthritis deformans or merely simulate that disease. There cannot, I think, be any doubt that in

some instances such changes, although they may closely simulate arthritis deformans, are due to thickening of the structures around the joint and not to the implication of the cartilages and bones; but on the other hand there are cases in which true arthritis deformans apparently takes its origin in joints which have been damaged by diseases of other kinds, and spreads from these to articulations which have previously escaped.

The difficulties encountered in attempting to arrive at a just conclusion are especially great when the chronic articular lesions occur as the sequelæ of an attack of acute rheumatism.

In the first place doubt may arise as to whether the original attack was actually one of acute or subacute rheumatism and not rather the more acute form of arthritis deformans, which in its earlier stages may, as has been already pointed out in a previous section, be easily mistaken for such an attack. The development of the signs of endocarditis or of pericarditis will, of course, afford evidence of the nature of the primary disease, seeing that such lesions are not met with in cases of genuine arthritis deformans; but it must be remembered that arthritis deformans is most likely to occur in persons who have reached a period of life when true rheumatism has far less tendency to implicate the heart than it has in earlier life. Other diagnostic signs will be the tendency of the joints first involved to recover quickly while new ones are involved, profuse sweating, and the tendency of the joint affection to yield quickly to the salicylic drugs. On the other hand persistency of the lesions and the affection of joints such as the temporo-maxillary articulations, which are little prone to acute rheumatism, speak strongly for the diagnosis of arthritis deformans.

Even when the rheumatic nature of the primary attack is beyond question, the diagnosis of the true nature of the secondary chronic arthritis may present even greater difficulties. There occasionally results from acute rheumatism a condition first described by Jaccoud and named by him "*rhumatisme fibreux*," which in its superficial aspects closely resembles arthritis deformans, and which is attended by fusiform enlargement of joints, and by similar muscular deformities; but in which no lesions of the bones or cartilages are found if the case comes to post-mortem examination.

In many instances the deformities are permanent, but when the acute attack has been recent, the fusiform swellings may improve remarkably in time, to the surprise of the medical attendant who has not anticipated any so favorable result. I have met with several cases in which this has been the course of events.

There are certainly many cases which cannot be referred to this

class, and in which, although the rheumatic nature of the original attack is beyond doubt, as time goes on the characteristic osteophytic outgrowths and other features of arthritis deformans make their appearance.

It is quite possible that in some such cases the damage done to the joints by the acute rheumatism is not really the starting-point of the deforming lesions, but that rather the subsequent arthritis deformans stands in the same relation to the febrile attacks as it sometimes does to other febrile disorders, such as influenza, which do not implicate the joints.

The following was one of the most typical examples of post-rheumatic arthritis deformans that have come under my notice:

The patient, a woman, aged 34 years, had first suffered from rheumatic fever when 11 years old, and had had two subsequent attacks at the ages of 18 and 24. Since then she had suffered from three attacks of moderate severity, since the last of which she had never been free from articular pains and had noticed enlargement of the finger-joints, which presented the typical appearance of arthritis deformans. There was marked ulnar deflexion of the fingers.

In addition to the finger-joints the knees, feet, ankles, wrists, shoulders, and elbows were more or less seriously involved. There was pain in the lower part of the back, but no stiffness of the neck nor of the temporo-maxillary joints.

The rheumatic nature of the original attacks was demonstrated by the presence of well-marked signs of mitral regurgitation.

In another instance a woman, aged 39, came under observation with the characteristic lesions of arthritis deformans. She had suffered from no less than four attacks of rheumatic fever, after the last of which the deforming changes had developed. She also had well-marked signs of mitral regurgitation.

Just as after rheumatic fever so after gonorrhœal rheumatism the articular lesions of arthritis deformans may be developed, and may extend in time to other joints besides those which were implicated as the result of the gonorrhœal attack.

A number of authors have recorded cases of this kind, but here again it is necessary to be on one's guard against mistaking for examples of arthritis deformans cases in which ankylosis of joints and considerable deformities resulting from the gonorrhœal rheumatism itself may more or less closely simulate that disease. Some at least of the recorded cases are not beyond question on this account.

In the following case the disease from which the patient was suffering when seen was undoubtedly arthritis deformans, as far as a certain diagnosis can be arrived at by purely clinical methods, and the evidence of the patient's regular attendant left no room for doubt that the original arthritis, although separated by a considerable in-

terval of time from the original gonorrhœal infection, was of gonorrhœal origin.

The patient was a young man, 27 years of age, who until three years previously had never suffered from any joint affection. Some six months after an attack of gonorrhœa, while he was still suffering from gleet, he developed an affection of one knee-joint which was attended with much pain and great swelling. There was no attendant affection of the eyes. The knee never recovered completely, and a year later many other joints became involved until he presented the clinical picture of multiple arthritis deformans in a most typical form.

I am not acquainted with any case of this kind in which the nature of the resulting joint disease was placed beyond all question by a post-mortem examination. Such cases are certainly less common than those in which a condition somewhat resembling arthritis deformans results from chronic changes in the joints which were the original seats of gonorrhœal arthritis, and perhaps the far greater liability of males to gonorrhœal arthritis, taken in conjunction with their far less liability to arthritis deformans, may be partially responsible for their rarity.

No one will question that in chronic gout osteophyte formation and ulceration of the cartilages may take place, but on the other hand many will call in question the propriety of speaking of these changes as due to the development of the lesions of arthritis deformans in joints damaged by gout. Certainly ulceration of cartilage may be connected with uratic deposits, and Ebstein even maintains that necrosis of the cartilages precedes the deposition of sodium bi-urate in them.

E. Wynne[66] has pointed out that the lipping of the bones observed in chronic gouty cases is due to a different morbid process from that which produces the similar lipping in arthritis deformans. He finds that in gouty lipping the cartilaginous covering ceases at the summit of the outgrowth instead of completely clothing it, and that over the remainder of the projecting part there is an investment of dense fibrous tissue, which is continuous with the periosteum and synovial membrane. He looks upon the outgrowths in such cases as true exostoses rather than as osteophytes.

The view taken as to the relation of these changes to the original gout will differ according to the views held as to the nature of arthritis deformans. If with Mr. Hutchinson we look upon the latter disease as a product of the admixture of gout and rheumatism, we may regard the supervention of these lesions as due to the importation of a rheumatic element into the case; and if, on the contrary,

we look upon arthritis deformans as a dystrophic change in joints, we may readily suppose that such dystrophy may affect joints which have been the seats of long-standing or often-repeated gouty inflammation.

Localized Arthritis Deformans.

The localized variety of arthritis deformans differs from the multiple in several remarkable respects.

In the first place it affects men more frequently than women; secondly, it attacks the large joints rather than the small, the most central rather than the most peripheral.

It is met with in its most typical form as the hip-joint disease of elderly men, and it was from the post-mortem examination of cases of this affection, the morbus coxæ senilis, or chronic rheumatic arthritis of Adams, that the complete picture of the morbid anatomy of arthritis deformans was originally drawn.

Very many cases of this affection have their origin in some injury, slight or severe, to the parts in the neighborhood of the hip-joint, and it is to this variety that one looks for the best examples of such traumatic origin.

The disease shows little tendency to spread, but the immunity of other joints, although the rule, is by no means constant, and it is not very uncommon to meet with Heberden's nodes in association with the hip-joint disease, or a slighter involvement of the opposite hip, with or without some associated affection of the lumbar spine.

The earliest symptom is pain and stiffness on movement. The pain is of a gnawing character, and like the pain of the acute hip disease of children often extends down the thigh to the knee.

Sciatica is the affection with which morbus coxæ senilis is most liable to be confused, but the difference in the situation of the pain of sciatica, the local tenderness over the inflamed nerve trunks, and the extension of the pain right down to the foot, usually deprives the diagnosis of any serious difficulty.

When doubt arises the patient may be subjected to the following tests: When a sufferer from arthritis deformans in the hip-joint is requested to cross the affected leg over the sound one, while in the sitting posture, he experiences much difficulty in doing so and is usually obliged to raise the thigh with his hands and lift it over the other one. Again when the patient stands upon the sound leg and attempts to rotate the foot of the affected side, there is found to be considerable limitation of the rotatory movement at the hip-joint. A further test is to place the patient in the recumbent position and to

deliver a sharp push upon the sole of the foot. This proceeding will cause pain in a diseased hip-joint, but not in the case of sciatica unless from the jarring of the limb.

Flattening of the buttock and wasting of the thigh of the affected side is a prominent sign of hip-joint disease, as distinguished from the wasting of the limb as a whole sometimes seen in cases of sciatica of some standing. The knee jerk on the affected side is as a rule markedly increased. In a word, the wasting conforms to the usual type of arthritic muscular atrophy.

As the disease progresses the abrasion and absorption of the head of the femur is apt to lead to a considerable degree of shortening of the limb, and in some cases the shortening is extreme.

Occasionally cysts of enormous size are developed in connection with chronic arthritis deformans of the hip-joint, and these are sometimes situated so far from the joint itself as to have no obvious connection with it. Similar cysts are sometimes met with in association with other joints besides the hip, such as the shoulder, elbow, and knee.

Morrant Baker,[67] who first described these cysts, holds that the synovial fluid which has accumulated in the cavity of the joint, having reached a certain degree of tension, makes its way out of the joint, in the direction of least resistance, either by the channel through which a normal bursa communicates with the joint, or by forming a hernia of the synovial membrane. Ultimately, if the tension continues to increase, the fluid escapes from its sac and accumulates in a cavity the boundaries of which are formed by the muscles and other tissues of the part.

It is not always possible to make out the presence of a communication between the cyst and the joint cavity during life, but it is certainly unsafe to argue from the failure to detect any such communication that none exists.

Next to the hip the shoulder and knee are the joints most frequently attacked by the localized form of arthritis deformans. One shoulder or both may suffer, and as in the case of the hip affection the lumbar spine may be involved in the disease, so the shoulder affection may be accompanied by spondylitis of the cervical or dorsal spine.

The movements of the joint are greatly limited, and in the earlier stages there is cracking, in the later grating on movement. There is seldom any effusion into the joint, but enlargement due to osteophyte formation may be made out when the disease has existed for some time, and, as has been already mentioned, the mechanism of the articulation may be reversed, the glenoid cavity being converted into a

convex boss, the head of the humerus into a cup. The adjacent muscles including the deltoid undergo conspicuous atrophy, and such arthritic atrophy of the muscles of the shoulder must be distinguished from progressive muscular atrophy. This distinction is usually a matter of no difficulty, the affection of the joint being revealed by crackling and by limitation of movement, which, even in the earlier stages of the disease, is conspicuously seen when the attempt is made to raise the hand to the head.

There is a peculiar type also common in men in which the disease is limited to the carpo-metacarpal joints of both thumbs. The enlargement of these joints is easily made out, and crackling and creaking on movement are readily detected. In the cases which I have seen, the onset of the disease has usually appeared to be referable to some occupation in which the thumb is much used, so that the joints in question are subjected to strain.

Joint Lesions Resembling those of Arthritis Deformans.

This is not the place in which to give any detailed description of the various forms of joint lesions which in their clinical aspects and morbid anatomy more or less closely resemble arthritis deformans, although they are not included under that name. On the other hand, were they not to be referred to, a group of facts which serve to throw important light upon the nature and origin of arthritis deformans would be omitted, and I therefore propose to give such a short account of these forms of arthritis as may serve to demonstrate the similarity of the several lesions.

The joint lesions above referred to are almost exclusively met with in connection with organic diseases of the nervous system. In connection with such nervous lesions forms of arthritis sometimes develop which in their clinical features more closely resemble those of gout or acute rheumatism, and which tend to pass away under treatment; again in connection with hemiplegia, cervical pachymeningitis, and other conditions, stiffness of the small joints of the hands with or without enlargement occurs, which is probably due to disorders of the nutrition of the parts; but the closest approach to the phenomena of arthritis deformans is presented in certain cases of organic disease of the spinal cord, such as locomotor ataxia and syringomyelia.

Charcot's Joint Disease.—Ever since attention was first called by Charcot to the association with locomotor ataxia of a form of joint disease which now usually bears his name, it has been recognized that although this arthritis presents, in its sudden onset and certain other clinical aspects, obvious differences from arthritis deformans,

in its morbid anatomy it presents obvious and close analogies with that disease. Indeed there can be little doubt that before Charcot's discovery such lesions were habitually assigned to that category.

Such anatomical differences as separate the two groups of lesions are differences of degree rather than of kind, and the most conspicuous of them is the far more rapid and extensive destruction of bone which contributes largely to the extreme laxity and disorganization of the affected joints. On the other hand the tendency to the formation of osteophytic outgrowths is decidedly less pronounced in Charcot's joint disease than in primary arthritis deformans. The destruction of cartilage is a feature common to the two conditions, as also are the changes of the synovial membrane, viz., thickening and the formation of villous outgrowths.

With Morrant Baker we may look upon the osteophyte formation as an attempt at repair, and may express the difference between the two conditions, by saying that in the arthropathy of locomotor ataxia the destructive far outstrip the reparative processes, whereas in osteoarthritis a more even balance is maintained.

The arthritis of syringomyelia presents quite as obvious resemblances to arthritis deformans as does that of locomotor ataxia. An important case of this disease was recently described before the Clinical Society of London by Dr. Beevor and Mr. Lunn,[62] which was under observation for ten years and eventually came to an autopsy. Some of the diseased joints were examined by Mr. Targett, who thus describes the condition of the left shoulder-joint:

"The anterior half of the glenoid cavity was entirely worn away and a new socket for the head of the humerus was formed upon the front of the neck and subscapular fossa. The margins of this socket were largely composed of new bone. The head of the humerus was likewise misshapen, being flattened considerably from before backward; its surface in contact with the scapula was largely deficient of cartilage, and in places eburnated, while that opposed to the capsule of the joint was much nodulated. Movements in this articulation were apparently very limited. As regards the interior of the capsule and the articular surfaces generally the aspect was that of osteoarthritis. The synovial membrane was beset with villous processes, and imbedded in the fibrous tissue were the usual additamentary bones."

In this case no question arose of the accidental association with the spinal lesions of primary arthritis deformans.

Joint Lesions in Hæmophilia.—There must not be omitted from the category of conditions which in their morbid anatomy more or less closely simulate arthritis deformans, the joint lesions to which

members of families in which hæmophilia prevails are subject, and which contribute largely to the sufferings of bleeders. These changes have been carefully studied by Bowlby,[39] who has shown that the changes met with in the articular structures cannot be attributed in their entirety to the mere effusion of blood into the synovial capsule.

In these cases, as in arthritis deformans, the cartilaginous covering of the articular ends of the bones becomes fibrillated, and in consequence assumes a velvety appearance; while in those parts which are most exposed to friction the cartilage becomes completely removed.

There is, moreover, the same tendency to the formation of cartilaginous outgrowths or ecchondroses, which, in time, become converted into osteophytes, surrounding the edges of the articular surfaces.

In certain respects, however, the arthritis of bleeders differs remarkably from true arthritis deformans. In the first place the joint cavity may, and often does, contain effused blood, and extravasations are frequently met with in the substance of the synovial membrane. Secondly, there is a great tendency to the formation of fibrous adhesions between the articular surfaces, which very greatly limit the movements of the affected joint, whereas, as we have seen, there is no tendency whatever to the formation of such adhesions in cases of true arthritis deformans.

Pathology.

The question of the pathology of arthritis deformans is one to which very different answers, all more or less tentative, have been and are still returned, and it is obvious that there is ample room for differences of opinion upon this point, seeing that the joints may suffer in a great variety of diseases of widely different types.

Arthritis is among the most conspicuous manifestations of certain infectious diseases, such as pyæmia and tuberculosis. In this class also the so-called gonorrhœal rheumatism must be included, and there is much evidence short of actual proof that acute rheumatism itself is due to a micro-organism.

Then, again, forms of arthritis are met with in the course of certain other acute fevers, in which, however, they play a very minor rôle.

Secondly, the arthritis of gout is constantly associated with the deposition of an abnormal chemical product in the articular structures, and there is much reason to think that we have here to deal with a form of arthritis dependent upon a derangement of the chemical processes of the body.

Thirdly, arthritis may result from an injury, as in the case of the common traumatic synovitis of the knee.

Fourthly, there is a group of arthritides which are associated with the various diseases in which hemorrhage is a conspicuous symptom, such as hæmophilia, scurvy, and the various forms of purpura.

Lastly, there are those interesting joint lesions just discussed which have their origin in connection with various disorders of the nervous system, and are almost certainly due to disturbances of the nutrition of the parts to which such disorders give rise.

It is *primâ facie* probable that in one or other of the above groups arthritis deformans should find a place, and the time has now come for the consideration of the argument for and against its inclusion in any one of them.

The chief views as to its nature which have up to now been advanced may be enumerated as follows:

1. That the disease is nothing more nor less than a variety of chronic rheumatism;

2. That it is a disorder of mixed pathology, a hybrid so to speak, resulting from the admixture of rheumatism and gout;

3. That it is largely of traumatic origin, resulting from mere wear and tear of the joints;

4. That in many instances the disease known as arthritis deformans is nothing more than a senile change;

5. That the joint lesions are of dystrophic nature, and are dependent upon disorders of the nervous mechanism which controls the nutrition of the joints.

It should be pointed out that of the five views above enumerated, the first and second look upon arthritis deformans as a systemic disorder of which the articular lesions are manifestations, while the last three do not involve the supposition of a general disease, but deal only with lesions of the joints, and of other parts the nutrition of which is liable to be simultaneously affected.

What may be styled, for the sake of brevity, the rheumatic theory has held a prominent position all through the history of our knowledge of arthritis deformans. This was the theory of Charcot and of Trastour, and has been adopted almost universally by the members of the French school, at any rate up to quite recent times.

At the present day it still has many supporters, and is backed by such an amount of powerful authority that its claims deserve most careful consideration, and cannot be lightly set aside.

It is a fact which cannot be denied that multiple arthritis deformans in its most typical form may follow an equally typical attack of acute rheumatism, and, as we have already seen, Sydenham clearly

described this order of events; but the value of any argument based upon this is seriously impaired by the equally indisputable fact that in the great majority of instances, a majority compared with which the number of the post-rheumatic cases sinks into insignificance, arthritis deformans has its distinctive characters from the first, being developed *de novo* without any antecedent rheumatic attack. Moreover, as we have seen, acute rheumatism is not the only disease affecting the joints of which arthritis deformans may occur as a sequel.

Other arguments which have been brought forward in support of the rheumatic theory are based upon the part played by cold and damp in the causation of the disease, and the association with the joint lesions of visceral and other affections similar to those met with in connection with true rheumatism. Both of these subjects have been already dealt with at some length, and it is only necessary to repeat here that I believe that the influence of cold and damp in the causation of arthritis deformans has had undue stress laid upon it; and that the endeavors to prove the occurrence in association with this disease of the abarticular lesions of rheumatism have resulted rather in the demonstration that arthritis deformans is not attended by any visceral lesions other than such as may be regarded as intercurrent disorders.

An exception should perhaps be made in favor of the subcutaneous rheumatic nodules, but, as was pointed out in speaking of these, our knowledge of the nodules themselves and of the nature of the joint lesions with which they are associated is not yet sufficiently complete to allow of any definite conclusion being drawn from their occurrence. It must, however, be admitted that at first sight the development, in association with apparently typical cases of arthritis deformans, of excrescences so strangely like those which have been regarded as pathognomonic of the true rheumatic process does supply a powerful argument in favor of the rheumatic theory.

The argument from the absence of visceral lesions loses some of its force from the fact that arthritis deformans is most apt to commence at a period of life when true rheumatism loses much of its tendency to attack the heart, and is apt to limit its activity to the joints alone; but the immunity from cardiac complications is quite as conspicuous in those cases in which arthritis deformans is developed in early adult life and even in childhood, if we exclude those instances in which it appears as a sequela of acute rheumatism.

Those who regard arthritis deformans as a form of chronic rheumatism have to admit that the chronic joint lesions which follow upon the more acute forms of that disease have more commonly a different character, that as a rule the destruction of cartilage and ten-

dency to the formation of bony outgrowths is wanting, fibrous ankylosis and thickening of the joint capsules being the changes more usually observed. In such cases the superficial resemblance to arthritis deformans in its early stages may be very close, but if, as is fortunately very seldom the case in the earlier stages of the affection, the case comes to a post-mortem examination, on cutting through the greatly thickened capsule the cartilages and articular ends of the bones are found intact.

While we are still ignorant of the nature of the *materies morbi* of acute rheumatism the question under discussion cannot be settled once and for all by an appeal to its constant presence or absence in cases of arthritis deformans; and we must continue to rely solely upon circumstantial evidence for the solution of the problem. To me such evidence as is forthcoming in favor of the contention that this malady is a form of chronic rheumatism appears to be greatly outweighed by that which is opposed to this contention, and especially by the evidence, presently to be discussed, which tells in favor of a quite different origin.

The theory which regards arthritis deformans as a mixed disease resulting from the blending of rheumatism and gout, which is identified with the name, and supported by the great authority of Jonathan Hutchinson,[70] is intimately mixed up with the hypothesis of the existence of an arthritic diathesis, which serves as a basis upon which rheumatism and gout and also articular disorders of other kinds may be developed.

Modern pathology has tended to drift away from the notion of such diatheses which held so prominent a place in the writings of French medical authors in the earlier part of the century. Possibly it may turn out that we have gone too far, and the pendulum may swing back again toward the older ideas. It is indeed probable that it will so swing back, to this extent at any rate, that more attention will be paid in the future than has lately been the case to the influence of the tendencies and peculiarities of the individual in modifying the course and features of any disease to which he may fall a victim.

It must be acknowledged that the more one studies the diseases in question the more one is struck by the peculiar way in which they are sometimes associated in a family, and it is difficult to reconcile such instances with the obvious and conspicuous differences which they otherwise present, and with the evidence which points to the possession by each disease of an entirely distinct pathology, and to their inclusion in quite different groups of diseases. For example, the apparent liability of the daughters of gouty parents to arthritis

deformans, to which reference was made earlier, lends support to Hutchinson's views; but on the other hand all that has been said against the rheumatic theory applies equally to this one, and we have the fact observed by Sir A. Garrod that no excess of uric acid is to be detected in the blood of patients suffering from arthritis deformans, and the point upon which Sir Dyce Duckworth has laid stress, that arthritis deformans is common in countries in which true gout is practically unknown.

The deposition of sodium bi-urate is a constant feature of gouty arthritis, but such deposits are not met with in the joints of sufferers from arthritis deformans unless there has been an antecedent attack of true gout; and if we once abandon the notion that uratic deposits and the presence of uric acid in the blood are necessary elements of gout, we abandon almost the only facts yet established by the study of the pathology, still so obscure, of that disease.

Taking all these points into consideration, it is difficult to suppose that a malady which lacks the distinctive features of both rheumatism and gout should yet be the product of the blending of those two diseases.

The wear-and-tear theory of Arbuthnot Lane, which is based upon the great destruction of the cartilages and bony surfaces, and the grooving of the latter in the lines of the articular movements, is obviously incapable of explaining the multiple form of the disease, in which we find the hand-joints early attacked, often in those who have never done hard work of any kind, and in which the lesions show a remarkable tendency to symmetry; and its author now admits this. On the other hand the appearance of the joints post mortem shows that when the articulations are once attacked by the disease, wear and tear plays a prominent part in the production of the observed lesions.

There is every reason to believe that, as Pye Smith[71] thinks, the disease is sometimes of the nature of a senile change in the affected joints; in other words, that it is the articular expression of the tendency of the tissues of old people to undergo degenerative changes.

There remains to be considered the theory which has gained many adherents of late years, which looks upon the joint lesions of arthritis deformans as dependent upon nervous influences reflex or otherwise, in other words as dystrophic in their nature.

No other argument which has been brought forward in support of this view approaches in cogency to that which is based upon the close similarity of the lesions of arthritis deformans to those found in certain forms of articular disease which are developed in the course of organic diseases of the nervous system, such as locomotor ataxia and

syringomyelia, and which are generally if not universally held to be dystrophic in their origin. The resemblances and differences between the conditions thus brought into comparison have been already discussed and it is not necessary to describe them further, seeing that their likeness to each other is questioned by none; so that we may take as established the first point in the chain of argument in favor of the theory, viz., that the changes in the joints to which arthritis deformans gives rise are such as are known to result from diseases of the nervous system which tend to impair the nutrition of the articular structures.

The remarkable symmetry observed in the distribution of the lesions in the multiple form of arthritis deformans, a character upon which Senator lays special stress, is also most readily explained by the supposition of a nervous origin. As we have seen, the degree of symmetry attained to is much greater than in other forms of articular disease, but unless we are prepared to assign all symmetrical diseases to such influences or at least to suppose that the distribution of the lesions is controlled by the nervous system, we must be careful not to press this argument too far. We must not forget that the subcutaneous fibrous nodules of young rheumatic patients, and various forms of skin disease which are not, like herpes zoster, obviously closely dependent upon nervous lesions, are apt to exhibit a curious symmetry of distribution, which may sometimes be comparable to that shown by arthritis deformans; nor that in locomotor ataxia at any rate the joints are not particularly apt to be symmetrically invaded, although in some other types of organic nerve disease corresponding joints on the two sides of the body, including the small joints of the hands, are apt to suffer.

The early invasion of the peripheral joints and the general tendency of the disease to progress centripetally is another feature of the disease which is easily reconciled with a nervous origin.

Further, the consideration of the etiology of arthritis deformans shows that its causes are such as might reasonably be expected to give rise to a nervous affection, rather than to a systemic disorder of some other kind.

Lastly, when we study the changes in structures other than the joints which are associated with this form of arthritis, we find that the visceral lesions which often play so conspicuous a part in blood disorders are conspicuous by their absence; whereas the changes in the muscles, skin, and other parts are for the most part of a dystrophic type.

The conspicuous atrophy of muscles is doubtless of this nature; but, as I have attempted to show, these changes are certainly to some

extent secondary to the joint changes and attend upon arthritis of all kinds both acute and chronic.

But careful observers have maintained that in arthritis deformans there is something more than mere arthritic muscular atrophy, and that to some extent at any rate the muscular wasting is not merely secondary to, but advances *pari passu* with the articular disease, and may even be met with in parts in which the joints do not as yet show any signs of being implicated.

Dystrophy of the skin is certainly observed in some cases, as well as disturbances of cutaneous pigmentation and local sweating which are recognized phenomena of nervous disorder, as are also the tingling and numbness of the hands and feet which are not uncommon early signs of arthritis deformans.

The most forcible objection to the nervous theory is the absence of any anatomical evidence of disease in the spinal cord to which the dystrophy of the joints can be attributed.

Changes in the peripheral nerves have been found by MM. Pitres and Vaillard in cases of arthritis deformans, and these may play some part in the causation of the cutaneous and muscular changes at least. The observers found that in a case in which muscular atrophy was very marked the muscular nerves were profoundly affected, whereas in a second case, in which the atrophy was slight, they exhibited no evidences of neuritis. The nerves supplying the diseased joint were but little affected, and MM. Pitres and Vaillard consider that the joint lesions themselves cannot be ascribed to this cause.

M. Ord believes that a reflex theory best explains the observed phenomena, and that the uterus is very frequently the organ from which proceed centripetal influences which are reflected along the same paths as those which in primary diseases of the spinal cord lead to affection of the joints. In support of this he brings forward evidence of the important part played by uterine disorders in the causation of arthritis deformans, and suggests that predisposing conditions such as debility and anæmia may assist this reflex process by increasing the morbid reflex excitability of the spinal cord provoked by the uterine disorder.

It is obvious that the dystrophic theory of arthritis deformans, although it appears to me to afford the best explanation of the phenomena of the disease, cannot as yet be looked upon as firmly established, in the absence of further evidence in its support from the side of morbid anatomy, and this obliges us to fall back upon the hypothetical explanation of a functional disturbance of the trophic influences of the nerve centres.

However, although an hypothesis, it is a satisfactory working hypothesis, which offers an explanation such as no other theory yet suggested can do, of the development of lesions of identical anatomical character under widely different clinical forms.

If in arthritis deformans we have merely a dystrophy of joints associated with dystrophic changes primary and secondary in other structures, it may easily be supposed that such dystrophies will sometimes be local, limited to a single joint which may or may not have been the seat of injury, may occur in very chronic forms in the course of senile decay, or under depressant conditions may assume a more generalized form attacking many joints, and adopting a more or less symmetrical distribution.

Treatment.

In advanced and in very chronic cases of arthritis deformans it is usually impossible to bring about any material amendment in the patient's condition, and our treatment must be chiefly directed to the palliation of his sufferings. This is, however, by no means the case when the patient is comparatively young, and when the disease is still in an early stage, for under these circumstances marked improvement under treatment may certainly be looked for, although it can never be confidently promised, seeing that not infrequently the morbid process continues to advance in spite of every endeavor to stay its progress.

In the general treatment of arthritis deformans two main principles need to be borne in mind, viz.:

1. That this is a disease which tends to attack persons whose vitality is lowered and who are in popular phraseology "run down," and that any lowering course of treatment, even if apparently beneficial for the moment, tends to favor the progress of the malady;

2. That any treatment, in order to be effectual, must be steadily persevered in for a long time.

No greater mistake can be made than that of treating the sufferers from the disease under consideration as if they were the victims of gout. The carefully regulated diet, with a limited supply of animal food which experience has shown to be beneficial in gouty cases, is positively injurious to patients with arthritis deformans, who require a diet as nourishing as their condition allows; and drugs such as colchicum and alkalies, which are usually prescribed for the gouty, are worse than useless in cases of arthritis deformans, while the patients derive benefit from tonics.

Good hygienic conditions; the removal as far as possible of busi-

ness and other worries; removal from a damp house or neighborhood; the taking of such amounts of recreation and exercise as are compatible with the sufferer's state are all important elements in the treatment. Indeed it is probable that change of air and scene not infrequently contribute materially to the benefit derived from a visit to some mineral-water resort.

The patient should reside in a mild but not relaxing climate, preferably away from the sea, for sea air usually tends to aggravate the articular and other pains. Dampness of air and soil should be avoided, and woollen clothing should be worn next the skin both in summer and winter. A winter residence in a warm climate in which the fluctuations of temperature are not extreme is often very beneficial.

In the acute stages and when there is much febrile disturbance a light but nutritious diet should be prescribed, but in the more chronic stages of the disease, if any rules are laid down as to diet, those articles should be specially selected which are likely to agree best and are at the same time nutritious. Meat should by no means be avoided, but the patient should be recommended to take nitrogenous food freely.

If the patient is accustomed to take some wine with his meals he may continue to do so, and a glass of stout at midday may often be prescribed with advantage if it can be taken without discomfort.

It is obvious from what has been said that when dyspepsia is present as a complication it is important to treat this condition which tends to interfere materially with the nutrition of the patient, and it is sometimes advisable, before commencing any other line of treatment, to devote our efforts to getting the stomach into better order.

These rules are not based upon any theoretical considerations as to the supposed nature of the disease, and in laying them down I am merely echoing the opinions of physicians who have made this disease the subject of a lifelong study, and who have formulated them as the outcome of a ripe experience. Of their correctness no one who has had opportunities of comparing the progress of cases in which they have been followed with that of others treated upon the opposite plan can entertain any doubt.

It is particularly in the matter of treatment by drugs that the necessity of persevering steadily in any plan which is adopted becomes most obvious, for even in the cases in which the effects of drugs are most marked no improvement is to be looked for from day to day, and the disease may even appear to progress unchecked for some weeks or even for a month or two before the case takes a turn and improvement becomes manifest. It is probably because these

facts are not sufficiently appreciated that many look upon the treatment of arthritis deformans by drugs as so hopeless, and that in so many cases one drug after another is tried in quick succession and without apparent benefit.

The drugs which are most in repute in the treatment of this disease are iodine and the iodides, arsenic, and cod-liver oil.

Free iodine may be administred in form of tincture in sherry, or solid iodine may be included in a pill. Iodide of potassium is much employed, but the long continuance of such treatment is open to objection, and iodide of iron, which is highly spoken of by Sir A. Garrod, is probably the best of the iodides in such cases. Its tonic properties are of great value in the treatment of arthritis deformans, and iron in any form is often of much value, especially in those cases in which anæmia is a conspicuous symptom. I have seen very remarkable improvement in some cases under the continuous administration of syrup of the iodide of iron alone for a period of six months or a year, and it is probable that the efficacy of this drug is increased by the addition of some preparation of arsenic. As to the efficacy of arsenic alone I cannot speak so positively, but I believe that it forms a useful adjunct to the iron treatment. It may be conveniently prescribed in the form of liquor sodii arseniatis with the syrup or as solid sodium arseniate with the pill of iodide of iron.

In the more acute cases quinine is sometimes given with advantage, but although the salicylate of sodium frequently affords some relief when the articular pain is very acute, I have never seen any marked or permanent improvement or the arrest of the disease result from its administration, and there are obvious objections to its continuous administration in large doses over a long period in such cases. Cod-liver oil forms a valuable adjunct to other remedies, and unless there is some reason to the contrary it should be taken continuously during the colder months. For those patients who are unable to take the oil as such, some of the various emulsions or preparations of cod-liver oil and maltine may be substituted. Other drugs which have been strongly recommended are the infusion of Fraxinus excelsior, Actea racemosa, and ichthyol.

It is not possible to prophesy in any given case how far a certain treatment will be efficacious. In a small proportion the improvement is very conspicuous, and if the disease is in its early stages a condition approaching to complete cure may be attained. In a far larger proportion of cases the disease appears to be arrested, no fresh joints become attacked, and those already involved became less painful and swollen; but in some instances our utmost efforts are powerless to arrest the progress of the morbid process. It is there-

fore necessary to watch the results of treatment during a period of several months before any sound prognosis can be safely given, and the patient should be warned that nothing startling in the way of amelioration is to be looked for.

In advanced cases with conspicuous osteophytic enlargement, and especially in those in which the deformities due to muscular contraction are already produced, little in the way of improvement can be looked for, and our efforts must be chiefly directed to the relief of the patient's sufferings. When the articular pain is intense salicylates may be tried for a short time, and relief may be obtained from local applications to the joints, such as belladonna and other liniments. Opium should be given with great caution in such a chronic disease, owing to the risk of establishing the opium habit.

In that form of intense pain which results from cramp, much relief is not infrequently obtained from the administration of hyoscyamus, which is sometimes completely effectual in relieving or in warding off the painful muscular contractions.

Thermal Treatment.—There can be no question that cases of arthritis deformans are among those in which decided benefit is often derived from a judicious course at some mineral-water resort, and it is from the external application of such waters that good results are to be looked for. The watering-place selected should therefore be one in which the treatment by baths is efficiently carried out; and the line of treatment which has in my experience proved most effectual is that which consists in massage combined with douching without the actual immersion of the patient. Ordinary immersion baths appear to me to be far less beneficial and if too frequently repeated to do harm rather than good. It would seem that in this disease the mode in which the water is employed is of more importance than its chemical composition, but at several of the places at which the most satisfactory results are obtained the waters are of the sulphurous class.

The douche-massage treatment originated at Aix-les-Bains in Savoy where there is an abundant supply of hot sulphur water, and the results there obtained are often extremely encouraging.

Aachen or Aix-la-Chapelle may also be mentioned among the continental bath-places which may be visited with advantage by these patients.

In England the arrangements for carrying out the Aix treatment are especially admirable at Bath, and here there is a large supply of a thermal water with abundant mineral ingredients. Harrogate, celebrated for its sulphur water, may also be mentioned among bath-places suitable for these patients, and Woodhall Spa in Lincoln-

shire, where the water is strongly saline and contains bromides and iodides.

Patients who prefer to go further afield may visit Hammam R'hira or Hammam Meskoutin in Algeria, or Halouan les Bains in Egypt. At these latter places there is the additional advantage of a warm and equable winter climate which may contribute materially to the cure.

Indeed a winter sojourn in such a climate as that of Egypt or the Canary Islands should be mentioned as in itself a valuable therapeutic measure in cases of arthritis deformans which have not reached too advanced a stage.

Many of the American spas and climatic resorts will be found efficacious in such cases. It is important that the patients should not be subjected to any course of treatment which tends to have a debilitating effect, for such treatment has in the long run the inevitable result of aggravating rather than arresting the malady. General vapor baths come under this head. When taken they undoubtedly afford a temporary relief and enable the patient to move with more freedom, but this relief is dearly bought at the expense of a deterioration in the sufferer's condition which results when they are repeatedly taken.

This does not apply to the Berthollet local vapor baths, which are applied to separate limbs or portions of limbs by means of specially constructed apparatus, and which sometimes form a valuable adjunct to other methods of thermal treatment.

In some cases in which other treatment fails, electric baths may be tried. A copper plate connected with the negative pole of a constant-current battery is placed at the foot of the bath, and another similar plate connected with the positive pole is placed at its head. The head and shoulders of the patient are supported by a wooden frame across which webbing is stretched, which prevents the body from coming into contact with the metallic plate.

The bath should be taken under skilled medical supervision, and the patient should remain in it for ten minutes while a current from about forty No. 1 Leclanché cells is passed through the water. As an alternative arrangement the current may be reduced, and the negative pole may be connected with handles which are held by the patient.

The late Dr. Steavenson spoke of good results which he had had from this treatment in arthritis deformans, and it is worth trying in cases which do not yield to other means; but I cannot say that in the cases in which I have watched the effect of electric baths in arthritis deformans, the results obtained have been very encouraging, perhaps because these have usually been cases in which other

modes of treatment have failed to give relief, and therefore hardly afforded a fair criterion of the value of the treatment.

A few words must be said about the local treatment of the affected joints. It is generally acknowledged to be undesirable to use such appliances as materially limit their movement, but in the more acute stages the patient may be unable to get about, and rest in bed or upon a sofa becomes not only advisable but even necessary. Dr. Kent Spender recommends that in such cases the joints should be supported, but not fixed, by mill-board splints. Wrapping in flannel bandages, sponging with hot water, or covering with hot sand according to a recommendation of Haygarth's, will sometimes afford relief, as also may the application of liniments as already recommended.

A moderate amount of rubbing is also sometimes useful.

In the more chronic stages the patients should be encouraged to get about, but such an amount of exercise as is followed by pain lasting for some hours should be regarded as excessive and should be forbidden.

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DISEASES OF THE MUSCLES.

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DISEASES OF THE MUSCLES.

THE study of diseases of the muscles is a subject that belongs at the same time to medical and to surgical pathology, and in an exhaustive treatise on these affections it would be necessary to consider them in both these relations. In the present article, however, I shall confine myself to the purely medical side of the question, leaving out of consideration those troubles which belong exclusively to the domain of surgical procedure. Among the latter are wounds, contusions and ruptures, diastasis, hernia, and tumors of various sorts which have their origin in muscular tissue. The parasitic diseases of the muscles, hydatid disease and trichinosis, will be treated of in the article on parasites in a subsequent volume of this series, and need therefore not be considered in the present treatise.

After passing briefly in review the general symptomatology of muscular affections, I propose to divide my subject into two main headings. In the first I shall consider all that relates to inflammation of the muscular tissue—myositis. The second part will deal with troubles arising from perverted nutrition of the muscles—trophic affections.

General Symptomatology.

We know that the muscles of the body are of two sorts—those of organic life, involuntary with smooth fibres, and voluntary muscles with striated fibres. The latter only will concern us here. The alteration in the muscular tissue may constitute in itself the entire disease, but most commonly it is encountered in connection with some general disorder. In the latter case the patient presents himself with all the symptoms of the primary affection to which are superadded the local signs due to the muscular lesion. When this lesion exists alone there are few general symptoms other than those due to the acute muscular phlegmasia. The patient has some elevation of temperature and loss of appetite, but only in that clinical form which will be described under the heading "acute primary infectious myositis" is the general condition one of alarming gravity.

As regards the local lesions, the diseases of the muscles present a

certain number of characteristics by which they may in general be readily recognized. These may be classified under physical and functional symptoms.

Physical Signs.—In every medical examination two of our principal means of investigation are inspection and palpation, and these are also the two factors by means of which we gain an idea of the morbid condition of a muscle or of a group of muscles.

By *inspection* we determine the size of a muscle, its form, and the coloration of the integuments covering it; by *palpation* we appreciate the changes in consistence and elasticity, and also learn what alterations of temperature, if any, there are in the part.

As regards volume, a diseased muscle may present various modifications; it may be increased in size, swollen, hypertrophied, or atrophied. In inflammatory affections of the muscles, either primary or secondary, we note most frequently a tumefaction, a swelling of greater or less extent, of the diseased part. It is not unusual also to find œdema of the overlying tissues. These are the phenomena associated with phlegmasic states. In chronic affections we may find atrophy or hypertrophy. We must, however, first eliminate that form of hypertrophy which is called physiological. Under the influence of exercise we often see a group of muscles attain a size much greater in proportion than that of other muscles of the body. This is because of its functional activity which leads to a greater supply of blood to the part and consequently increased nutrition. As instances of physiological muscular hypertrophy I may mention the large muscles of the right arm and leg of the fencing master, the hypertrophied biceps of the gymnast, the large calf muscles of the ballet dancer. But in this there is nothing pathological, and if certain muscles are developed out of proportion to others the only harm resulting is a loss of symmetry. Indeed, not only have the muscles preserved all their strength and vigor but they possess these qualities in even greater degree.

Pathological hypertrophy, on the other hand, is most commonly a false hypertrophy. The muscle has actually undergone a deterioration, a degeneration; it is no longer the powerful contractile tissue which imparts movement to the osseous levers, but it has been invaded by an inflexible, inelastic substance which gradually robs it of its distinctive properties. Pathological hypertrophy might therefore be regarded strictly as a simple atrophy.

Atrophy is a condition which often affects the muscles. They are then seen to be more or less diminished in volume; the normal prominences of the bony framework become more noticeable, and in advanced cases it is often possible to distinguish clearly all the con-

tours of the bones, the affected part presenting almost the appearance of a naked skeleton.

The altered coloration of the skin may attract attention. In acute diseases there is usually a redness of the integument of greater or less intensity.

Finally inspection enables us to appreciate deformity in the regions under the influence of the muscular trouble. As a result of inflammation the muscle may be shortened and retracted, giving rise to malpositions of the affected limb.

Such are the details which we may gather from a simple inspection of the parts. *Palpation* gives us information of no less value. In the first place we are enabled to detect modifications in consistence of the affected group of muscles. Under normal conditions the tissues which we are now considering have a very characteristic elasticity and firmness all their own, but in disease this firmness may be increased or diminished in more or less marked degree. Sometimes a sensation of resistance, which may amount even to hardness, is imparted to the touch; at other times, on the contrary, the muscle is soft and gives to the examining finger an impression almost exactly like that imparted by adipose tissue. The degree of softening may at times be even more pronounced, and the condition may go on to the formation of an abscess, when fluctuation will become manifest. Changes of temperature are frequently appreciable to the hand as well as by the thermometer. In acute myositis the parts are hot and burning, while in certain chronic affections on the other hand, in atrophic conditions for example, a reduced local temperature has occasionally been noted.

In order to complete this enumeration of the facts to be learned from physical exploration, we ought perhaps to mention direct *microscopical examination* of the diseased muscle. In certain cases of peculiar interest, we may extract a little piece of muscular tissue by means of a harpoon and examine it under the microscope. That is, however, a point of purely scientific interest, for the method is seldom of any practical clinical utility.

Functional Signs.—The two most frequent and most important symptoms are lassitude and pain. When the muscular system is affected the patients experience difficulty in movement, they complain of great weakness and heaviness in the limbs. I believe that in most acute infectious diseases the initial lassitude that is felt is often an expression of muscular inflammation. As the condition increases in severity pain is felt; the affected parts may be located by the tenderness elicited by pressure, or else the patient himself locates the disease by the more or less severe pain, occurring independently of pressure.

in one or the other part of the body. This pain may be of such intensity as to prevent absolutely all movement of a limb or of the segment of a limb. Functional impotence is therefore a result of the pain. But this may equally be due to degenerative changes. In pseudo-hypertrophic muscular paralysis, for example, the time comes when the lesions are so advanced that the patient is incapable of movement and is obliged to keep the bed. The same thing also occurs in lead palsy,—if it be admitted that the poison in this condition acts directly upon the muscle, the tendency now being rather to consider the toxic action as affecting the nerve terminations, to the lesions of which the paralysis is due.

As regards the functional symptoms nervous and muscular affections are often closely related, and in certain cases it may be difficult to determine the part taken by each of the two elements in the production of the symptoms. I do not propose to enter upon the domain of the pathology of the nervous system; hence in speaking of muscular contraction, a most common symptom, I shall concern myself only with that arising directly and solely from disease of the muscle itself. This condition of hardness and rigidity is occasionally produced as a result of inflammation—the best example which occurs to me being the affection of the sterno-cleido-mastoid muscle known as torticollis. From some cause or another this contraction may disappear and the function of the affected muscle be restored to the normal. It is not the same, however, with true contracture. This symptom is the expression of a sclerotic lesion and is consequently of much more sombre prognostic import than is simple contraction.

In the group of functional signs we may conveniently study the modifications of electrical contractility. By this term is meant the property which the muscle possesses of contracting under the influence of the electric current. It is necessary here again to distinguish between the direct action of the electricity upon the muscular tissue itself and that produced by the intervention of the nervous conductors. Duchenne and Remak have contributed largely to our knowledge of electrical muscular contractility. More recently Legros and Onimus have taken up the study of the subject and have presented conclusions of very great interest. It is probable that the last word on this subject has not yet been said, but however this may be, we are able by this mode of examination to obtain very valuable data concerning the functional capacity, the contractile power, of the muscle.

In conducting this method of exploration we may make use of two of the forms of electricity, continuous and interrupted currents, studying thus the galvano- and the farado-muscular contractility.

Whatever may be the kind of current employed the technique remains the same. The object is to influence the muscle directly, avoiding as far as possible all outside influences. That, it is hardly necessary to say, is an unattainable ideal, for it is impossible, under normal conditions, to dissociate completely the electrical excitability of the muscles and that of the nerves. This should not deter us, when studying the properties of muscular tissue, from making every effort to approach as near as may be to the ideal. It is to this end that it has been proposed to employ very fine needles as electrodes, one connected with the positive and the other with the negative pole. We might indeed obtain very exact results by inserting one of these needles at one of the points of insertion of the muscle and the other at another, and making the current pass between them, but this is a method that is not practically applicable.

In practice electrodes having quite a considerable area are employed and care is taken to wet them in a ten or twenty per cent. solution of chloride of sodium before they are applied to the skin. It has been taught that the electrodes should be applied at parts corresponding to the insertion of the muscles, and the current passing between them will then excite muscular contractions, the intensity and extent of which present variations of considerable interest. The following, however, is the method usually employed at the present day: An electrode of large area, known as the indifferent electrode, is placed upon the sternum; the other, the differential electrode, is brought in contact with the integument covering the muscle to be examined. The current passes and the circuit is then closed; when the electrode is removed the circuit is opened. I need not more than refer to the necessity that may exist for attaching to the exploratory apparatus an instrument for indicating the intensity of the current.

In order to simplify the recording of the modifications observed under the influence of the electrical current, it has become customary to employ a certain number of conventional signs, designating the positive and negative poles, the opening and closing of the current, and the reaction (shock or contraction) which results. But for all these details I must refer the reader to one of the numerous special treatises on medical electricity. We need only add that, after having tested the muscle directly by means of the negative pole, the corresponding electrode should be used as the indifferent one, the positive electrode then becoming the one by which the reactions are tested. By this substitution we may obtain differences in reaction of some diagnostic value.

In the normal state, the faradic current excites independent contractions when the interruptions are not very rapid; when these

are increased the muscle becomes tetanically contracted. The negative pole always produces stronger contractions than the positive. When we galvanize a healthy muscle we obtain weak localized contractions at the instant of opening or closing the circuit, and we note also that the negative pole excites to stronger contractions than the positive.

I have already spoken of the difficulty that is met with in dissociating electrization of the muscles from that of the nerves. We should take care not to place the electrode over the points of entrance of these nerves, a matter of relative ease in the case of certain muscles such as the biceps, the deltoid, the anterior muscles of the leg, etc. Furthermore the points of election for application of the electrode have been determined in the case of each muscle and are pictured in many works on the subject.

In disease of the muscles we often find a diminution or even a complete abolition of the electrical contractility. This abolition of reaction indicates a destruction of the muscular element. In certain cases there is, so to say, a dissociation of the electro-muscular contractility, and we find that the continuous current will still excite contractions while faradization produces no effect.

After this brief consideration of the general symptomatology of diseases of the muscles, in a certain measure necessary by way of introduction, we will take up the study of the various forms of inflammation of muscular tissue.

Myositis.

All writers who have concerned themselves with this question have remarked with justice upon the insignificant place that inflammations of the muscular tissue hold in pathology. Very often, indeed, these affections arise in the course of general diseases of which they are then but epiphenomena of slight comparative importance, and thus are thrown into the background. Nevertheless we cannot deny that there does exist a class of primary muscular inflammations in which the myositis is the sole lesion, all the other morbid symptoms being subordinate to this change.

I would then divide the myositides into two great classes according as the disease affects primarily and especially the muscular tissue, or as it attacks other organs first, involving the muscles secondarily. We therefore have the two main divisions of primary and secondary myositis. The former is divided into acute and chronic forms, and the first of these again is subdivided into acute simple and acute infectious myositis.

Primary Myositis.

We may say that the work of Pasteur and of his followers has thrown new light upon the entire field of medicine; and the chapter on myositis forms no exception to this statement. Indeed, the questions of its etiology and pathology have profited much from the light given forth by these remarkable discoveries. Up to that time we were only able to note the existence of an inflammatory condition involving a particular muscle or group of muscles, going on sometimes to suppuration, but we were unable to explain the reason for this particular localization independent of any general disease. Among the determining causes were mentioned cold and fatigue, but in that we had only one element of the problem. When, however, it was demonstrated that, in addition to these causes acting as depressants upon the organism, there was necessary a penetration of germs coming from without, or already present in the tissues and assuming a special virulence in consequence of the lessened resisting powers of the parts, then the second pathological element was found and an end was put to all the various hypotheses formerly in vogue. Some had described myositis as an inflammation of rheumatic nature; others, among whom was Grisolle, contented themselves with noting the fact of the inflammation, calling attention particularly to its infrequence. Finally, under the influence of the theories put forth by Tessier, myositis was grouped among the affections due to the purulent diathesis, and Dufresne (Paris, 1888) undertook to champion this opinion. Brunon, in his inaugural thesis (Paris, 1887) and in two subsequent publications (1890–91), elevated primary myositis to the dignity of a distinct morbid entity, and we may say that he has put the matter absolutely in its proper light. We may also mention the works of Strümpell, Hayem, Gluzinski, Larger, and many others.

Etiology.—Primary myositis is a comparatively rare affection. On this point all authors are agreed. It occurs generally in young persons. Among the alleged etiological factors two seem to be of real importance, viz., cold and fatigue. If we ask a patient suffering from acute myositis, whatever its intensity or location, how it was acquired, we shall usually learn that a short time before the disease made its appearance he was engaged in some very laborious undertaking, or endured some excessive fatigue—in a word, that he was overworked. Often also it will be learned that he experienced a sudden chill while perspiring, or that he was caught in a soaking rain. Such being among the active exciting causes, we ought not to be surprised at the greater frequency of primary myositis among soldiers

than among those in civil life. It is among recruits especially, who have not yet become accustomed to violent exercises, that myositis is most frequently observed. Constant rubbing, pressure, or contusions of a muscular region may also play an important part in the production of the disease which we are now considering. Next in order come mental disturbances and other influences which tend to depress the general condition, and finally may be mentioned malnutrition in consequence of insufficient quality or quantity of food. In a word any cause which weakens the resisting powers, and especially anything which also affects chiefly the muscular tissue, may act as an excitant of myositis. It is always the working muscles that are attacked.

But in addition to a suitable soil we must have the cultivation of the germ. It is very evident that in a field so well prepared by all the external factors which we have just mentioned, the micro-organism will find a soil very favorable to its development and growth. And this is, indeed, what occurs. Brunon succeeded in obtaining from the muscles of a person dead from primary myositis a certain number of microbes among which he found the streptococcus. The predominating rôle of micro-organisms in the pathogenesis of the inflammation is undeniable, and moreover it is often possible to prove that the person affected has been exposed for a longer or shorter period in a locality infected by the microbes of suppuration.

The micro-organisms transported by the blood take up their growth in the tissues which happen to offer them the least resistance, in the muscular tissues in the cases now under discussion, and especially in exhausted muscles.

I believe that primary myositis is not dependent for its production upon any single variety of microbe, but that on the contrary every pyogenic micro-organism or any that is capable of so becoming, may be arrested in the muscular tissue and excite there troubles analogous to osteomyelitis in osseous tissue. Among these micro-organisms I may mention the streptococci, which have been found in the diseased muscles by Brunon, the staphylococci, and the pneumococci.

Pathological Anatomy.—The muscle may present different appearances according to the degree of the inflammation and also to the length of time that this inflammation has existed. This is what has led various authors, and Hayem in particular, to describe several varieties of the affection based upon differences in the anatomical changes. The latter describes the hyperplastic, the calcareous, and the purulent forms of myositis.

When we examine a part affected by myositis we may often be struck by the lesions of the superficial structures. The skin and

cellular tissue may also be involved in the inflammatory process; and on making our incision layer by layer down to the diseased muscle, we frequently note œdema and inflammatory infiltration with abnormal vascularity of these parts.

The muscle itself presents different appearances according as it is or is not the seat of a purulent collection. We will consider first the cases in which no suppuration is present. The muscle is seen to be no longer of the bright red color characteristic of healthy flesh; its tint is darker, approaching more nearly to black, yellow, or gray. Its consistence has undergone profound modifications. It is no longer a firm resistant tissue, difficult to tear or to cut. It has become soft and friable and often exhibits a tendency to change into a pultaceous mass. Finally at autopsy we may find ruptures of the muscular tissue produced as a consequence of the inflammation. Where these ruptures have occurred there is seen to be an extravasation of blood, and not infrequently more or less extensive clots.

The microscope reveals an atrophy, or even a complete absence, of the striated fibres. The two principal alterations are granular and waxy degeneration. The connective-tissue elements proliferate; the embryonal cells become organized. Occasionally a cure is brought about either by the formation of a fibrous cicatrix or by the regeneration of the muscular tissue itself, as has been observed by O. Weber and Hayem. In this case the nuclei of the sarcolemma proliferate and give rise to embryonal muscular fibres which in turn gradually develop and end by replacing those destroyed by the inflammatory process.

But the course followed by a myositis, as regards its anatomical changes, is not always the same as here indicated. Under the influence of causes which it would be difficult to state with precision, among which we should have to take count of a special virulence of the infecting germ and a peculiar weakness of the soil, suppuration takes place. It is then especially that we see yellowish, grayish, or even greenish discoloration of the muscular tissue. Most frequently the formation of pus is preceded by ecchymosis and infiltration of the tissue with a black pitch-like blood. The pus contains, in addition to numbers of red blood corpuscles, a quantity of detritus coming from the connective tissue and from the disintegration of the muscular fasciculi.

The brief description which I have given applies to cases of acute myositis. When the inflammation passes into the chronic stage, the first sign that strikes the attention of the observer is the altered color of the tissue. The tint is much less pronounced; the muscle is no longer red, but rather pink or whitish. It is of greater consis-

tence. There is a peculiar induration of the part which is due to the fact of an abundant proliferation of the connective tissue at the expense of the muscular elements.

I ought also to mention the occasional formation of calcareous deposits in the substance of the muscular tissue.

Alongside of the lesions of the muscles, in a great number of cases we note other morbid localizations. The lungs may be congested, especially at the bases. Occasionally congestions of the liver and of the kidneys have been found, and in two cases reported by Brunon the spleen was soft, black, and increased in size.

Symptomatology.—This chapter is somewhat complex and I shall find myself obliged to divide it into several parts, in order to give a clear description of the different forms of primary myositis. This affection may present itself under one of two main forms, acute and chronic, which are very distinct one from the other in their symptomatology. We will begin with the former.

Acute Myositis.

We may describe here two forms—acute simple and acute infectious myositis. The latter again may be divided into two varieties: one, studied by Brunon, which is accompanied most frequently by suppuration; the other, studied by Hepp, Marchand, Larger (Thèse de Paris, 1890), and very recently by Gouget (*Presse Médicale*, September 1st, 1894) in which there is never any formation of pus.

Acute Simple Myositis.—This affection declares itself after a few indistinct prodromal symptoms. Following an exposure to cold or after excessive fatigue, the patient is taken with malaise and lassitude, and soon pains more or less severe are felt in the affected muscles. These pains, which are lancinating in character, are increased by pressure and impede voluntary movement. The position of the affected limb is often modified by the efforts of the patient to approximate as much as possible the points of origin and insertion of the inflamed muscle. As a consequence of the inflammation there may also be an actual shortening of the muscular fibres.

When the superficial muscles are affected the overlying tissues are changed in color, the skin being more or less intensely red and occasionally ecchymosed. We may also note œdema and swelling of the neighboring parts. When the muscles are sufficiently near to the surface of the body to be accessible to inspection and palpation, they may be seen stretched like tense cords under the skin, and they give to the finger an impression as of a hard body—a wooden sensation.

In mild cases it is doubtful if any general symptoms will be present, and if they are they will be found to be of slight importance. They consist in a slight rise in temperature, a little falling off of the appetite; but by the end of from two to fourteen days they will have all disappeared and the patient will be restored to his usual health. The pains will have also disappeared, and nothing will remain unless possibly a slight sensation of fatigue in the muscles that were the seat of inflammation. But the disease does not always have such a favorable and speedy termination.

More pronounced general symptoms may be present—fever, usually of moderate intensity, insomnia, and some gastric disturbance. The inflammation of the muscles lasts for from twenty-eight to thirty days, but then ends in resolution without suppuration. It may be, however, that the pains show no tendency to diminish; the general symptoms, without becoming really grave, show no amelioration; and in time the myositis passes into the suppurative form. Pus forms and collects, fluctuation appears, and a true abscess results. Such are the symptoms of simple acute myositis.

Acute Primary Infectious Myositis.—The course of this form of the disease is much less favorable than that of the variety just described. As was mentioned above, there are two forms of this variety of inflammation, of equal gravity indeed, but differing as regards the tendency to the formation of pus. In order to distinguish these two forms, I would call the first one, that in which there is a tendency to the formation of pus, "acute primary infectious myositis, properly so called," and the other form, that which runs its course without suppuration, "acute primary infectious polymyositis."

Acute Primary Infectious Myositis, Properly so Called.—This affection may begin in one of several ways. Sometimes, and most commonly, it is the general symptoms which first attract attention; at other times, and less frequently, the disease appears as an acute simple myositis. In the latter case the patient complains first of violent pains in the muscles, then the general symptoms become more and more severe and we find ourselves in the presence of an infectious myositis. In the ordinary variety the patient is suddenly taken, after some physical overstrain, with a chill or a succession of chills followed immediately by a fever of considerable intensity, reaching as high as 104° F. There is a general lassitude; the appetite is lost; and sometimes there is more or less stupor. While these general symptoms alone are present there may be some uncertainty in diagnosis, but this for a short time only, as soon the muscular pains begin to declare themselves and point clearly to the nature of the trouble. These pains, which are of varying degrees of

severity, tend to localize themselves in certain regions, principally in the muscles which have been overstrained. When the local disorder has become established, palpation, which may be exquisitely painful, reveals a wooden hardness along the course of the affected muscle, if the latter be superficially located. The skin, which presented a normal appearance at the beginning of the malady, is now covered with irregular patches of red discoloration. There is swelling over the region of the diseased muscles, and there may even be œdema of considerable extent. Finally the finger may detect a certain puffiness, or even fluctuation, if pus has formed. In these conditions the case is comparatively simple. Sometimes, especially when the disease attacks the deeper muscles, there are few or no local symptoms, and even pain may be absent. We may well understand how great is the embarrassment of the physician in such cases in arriving at a correct diagnosis.

As the muscular lesions take their course the general condition of the patient remains stationary. There is always considerable fever (103° to 104° F.), the tongue is dry, there is dyspnœa, the appetite is lost, there are abundant sweats, and in certain cases a vesicular eruption has been observed. These vesicles contain first a clear transparent fluid which gradually becomes milky, and then the vesicle dries up and a sort of epidermic desquamation follows. When the disease is going to take a fatal course, which is not infrequent, all these symptoms become aggravated: diarrhœa sets in, the teeth are covered with sordes, the patient is agitated, delirious, and finally falls into a condition of extreme exhaustion, and dies.

In certain favorable cases the general condition is never very grave; the symptoms are then referable chiefly to the stomach; the tongue is white, there is a bad taste in the mouth, but the temperature is usually not so elevated as in the class of cases previously described.

Infectious myositis, when occurring in its most grave form, may carry off the patient in five or six days; in less rapid cases death may ensue from the ninth to the sixteenth day. In favorable cases the symptoms gradually amend, the pains become less severe, the temperature falls, and the patient enters into the stage of convalescence. But this convalescence, like that of all infectious diseases, is always long and tedious, and for months the patient suffers from muscular pains and general weakness.

A remarkable fact in this variety of infectious myositis is the rapidity with which the pus is formed. In the very acute cases death may take place before we are able to discover the presence of pus or to adopt measures for its evacuation, and yet at the autopsy we may

find entire masses of muscular tissue transformed into abscesses. Pus has been found within three or four days of the onset of the disease. Suppuration is not, however, necessarily attended with fatal results, and patients have been known to recover after the evacuation of very large abscesses. When the course of the disease is more benign it may terminate by resolution; in this case the muscles generally remain more or less rigid for a considerable period of time, impeding in great part the movements of the affected limbs.

Primary Acute Infectious Polymyositis.—This disease, which has been studied by Unverricht, Marchand, Hepp, Larger, and Gouget, presents a clinical picture differing very markedly from that which we have just drawn. In this form suppuration never occurs, and furthermore the disease, instead of being localized in any muscle or group of muscles, involves almost the entire muscular system. But that is not all, and we shall see by a study of the symptoms and of the course of the disease that we have here to do with an independent morbid entity.

The prodromic period of acute infectious polymyositis may be very long. For weeks or months the patient may complain of fatigue and unusual lassitude, but in general this period lasts only from three to five weeks. The first manifestations of the disease are œdema, pain, and redness. The œdema, at first of slight extent and painless, is commonly localized on the extremities or the face. The redness, more or less pronounced, appears on the face, extremities, or abdomen. The erythema is seen, on examination, to be due to the presence of little spots, not elevated above the surface, more or less confluent, and disappearing on pressure. The pains gradually increase in severity, and the patient, who at first feels only an unusual fatigue and some gastric disturbance, is soon forced by the pain to take to his bed. It is at this time that the grave symptoms declare themselves. Occasionally they may be at their height by the end of from eight to twelve days, but usually their full development does not take place until, as we have seen, the expiration of from three to five weeks. At this time the patient often has a succession of chills and the temperature rises to, or exceeds, 104° F. The œdema becomes hard, and the pains grow so violent that the patient instinctively restricts all motion, and lies stiff and as if strapped to his bed. The muscles seem to be in a state of contraction, holding the limbs in semiflexion; they do not react to electrical stimulation. The tendon reflexes are abolished (Hepp).

Perspiration is most commonly very abundant; the urine is dark in color and sometimes contains albumin; the tongue is dry; the thirst is intense; constipation is the rule. The pulse is small, the

liver and spleen are enlarged, and very frequently lobar pneumonia is present. The latter is generally one of the later complications.

All the muscles are more or less affected; those of the thorax and of the pharynx lose their functional power, and the patient succumbs to exhaustion or to suffocation and asphyxia, a result to which the pneumonia often contributes.

In certain cases, unfortunately rare, after the disease has existed for a considerable period it may begin to recede, and the patients then enter upon a period of convalescence, which is always of long duration.

Chronic Myositis.

The symptoms of chronic myositis are often but slightly marked. The affection may follow an acute attack, or it may be chronic from the beginning. Careful palpation enables us to discover that the muscle is as it were thickened and at the same time painful. There may be difficulty in movement; sometimes we even find atrophy and resulting deformity.

The most interesting variety of chronic myositis is that which has been described under the name of *ossifying myositis*. We may distinguish two forms of this disease. The first is characterized by bony formations in the body of a muscle constantly exposed to slight injuries, such for instance as the abductor muscle in a cavalryman. The second variety is the disease studied by Münchmeyer and called progressive ossifying myositis. This affection, concerning the nature and pathogenesis of which we know but little, begins during later childhood, and is characterized by an ossification of the muscles, the process starting with those of the back of the neck. There is at first a swelling of this region, which swelling gradually disappears and is replaced by an indurated nodule. This process is repeated and the work of ossification goes on, invading in turn the muscles of the back, the neck, and the shoulder. As a rule the disease lasts not less than ten or twelve years, slowly progressing toward a fatal termination.

Diagnosis.—Simple acute myositis is an affection the diagnosis of which is easy. The pain limited to a certain muscular region, the prominence of the affected muscle above the surrounding surface, the wooden feeling imparted to the palpating finger, leave in general little doubt as to the condition present. The general symptoms, the fever accompanying pain in the extremities, may give rise to a suspicion of acute articular rheumatism, but in the latter disease the pain is most intense in the articulations, which are very evidently

distended with fluid, while nothing similar is seen in myositis in which the joints are unaffected.

The symptoms might also suggest a phlegmon of the cellular tissue, especially when a pulpy feeling or even fluctuation, indicative of suppuration, follows the primary induration. The shape of the affected region and the deeper situation of the bogginess felt on palpation will enable us to exclude a phlegmon.

In the case of primary infectious myositis the diagnosis may present greater difficulties, and because of the comparative rarity of the disease it is very possible for the physician to go astray. In the presence of the grave general symptoms observed at the onset of the disease one's attention may be turned away from the muscular system and directed to any one of a number of other organs. The violence of the fever, the loss of appetite, and the general depression may lead one to think of an eruptive fever or an acute articular rheumatism of malignant type. Thus it is necessary to eliminate cerebral rheumatism, typhoid fever, osteomyelitis, circumscribed phlegmon, pyæmia, suppurative arthritis, ulcerative endocarditis, etc.

In the case of polymyositis, the symptoms may suggest glanders or trichinosis; occasionally indeed the diagnosis from the latter affection is one of great delicacy. But it should be remembered that trichinosis begins usually in the muscles of the face and in the tongue, while in polymyositis it is the muscles of the extremities that are first attacked; furthermore, in trichinosis the disease is localized especially in the flexor muscles of the extremities, while on the contrary it is the extensor muscles that are principally affected in polymyositis.

In order to avoid confusion with the affections just mentioned and to establish a correct diagnosis, we must carefully study the progress of the disease; the patient should be examined with attention, the exact seat of his pain being noted; by palpation we may also arrive at an appreciation of the pathological condition of the muscles. But in spite of everything, in certain obscure cases in which the deeper muscles are the first attacked, we may be obliged to withhold a diagnosis for a time.

After having established the presence of inflammation of the muscular tissue, we have to determine the variety of myositis that is before us. And in the first place whether it is a primary or a secondary myositis—usually a matter of but little difficulty. If the patient is already suffering from some infectious disease (small-pox, typhoid fever, etc.) we must attribute the muscular inflammation to this infection. We ought also, in the case of an infectious myositis, to distinguish the particular variety with which we have to deal.

With this object in view we must bear in mind the distinctive points in the symptomatology above described.

In the case of chronic myositis it is sometimes difficult to determine whether we have to do with a primary myositis or with an inflammation of a rheumatic nature. Some writers, indeed, make no distinction between myositis and muscular rheumatism. We must also not forget that both syphilis and tuberculosis may produce an inflammation of the muscular tissues.

Prognosis.—Acute simple myositis usually terminates in recovery. Even when the inflammation proceeds to suppuration, the patient's condition is not necessarily serious, for after the evacuation of the pus perfect recovery may ensue. We may therefore regard this form of myositis as benign. It is very different, however, with infectious myositis. Here we are in the presence of a grave affection, and even when the symptoms are not of extreme severity we should always be reserved in our prognosis. The entire organism is infected and a cure is the exception rather than the rule. In the hyperacute cases the patient may be taken away within a few days, presenting symptoms of extreme exhaustion. Sometimes the disease progresses more slowly, but death follows just as surely. In a few more fortunate cases the general symptoms gradually subside and convalescence is established; but despite these exceptional occurrences the prognosis of primary infectious myositis should be regarded as of extreme gravity.

In the case of chronic myositis the question of death, at least of speedy death, does not enter into consideration. The disease may occasion deformity and functional impairment, but even the most dreaded form, that described above under the name of progressive ossifying myositis, advances very slowly. We can hardly look for a cure of this disease, but its progress is so slow that a fatal termination through exhaustion need not be anticipated under twelve or fifteen years.

Treatment.—The treatment to be adopted in the case of myositis will vary according to the form of the disease with which we have to do. In the simple acute form we should secure complete rest for the patient and immobilize as far as possible the diseased parts. At the beginning we may employ blood-letting under the form of wet cups, or mild revulsion obtained by applications of the tincture of iodine or by punctate cauterizations. If in spite of this the inflammation shows no tendency to subside we must envelop the parts in a moist antiseptic dressing. If pus forms it must be evacuated as soon as its presence is recognized. After the opening has been made the cavity must be carefully drained and washed out twice a day with a warm antiseptic solution, either of corrosive sublimate (1:2,000) or of car-

bolic acid (1:90). Under this treatment the suppurative process will gradually subside, and, the drainage tube being shortened each day, cicatrization of the entire cavity will eventually be obtained.

When a certain degree of rigidity of the muscle remains after an attack of acute simple myositis, or when more or less induration persists, the parts should be smeared with Neapolitan ointment. In the chronic forms, whether following an acute attack or chronic from the outset, we must have recourse to the continuous current or to massage. In the case of progressive ossifying myositis the only remedy that need be mentioned is the iodide of potassium.

In the case of simple acute myositis the general treatment is usually of secondary importance. For the relief of the pain and the fever we may give quinine, antipyrin, or some one of the other analgesic antipyretics. If suppuration occurs the strength of the patient must be maintained by tonics and stimulants, and the gastro-intestinal troubles must be combated by the administration of some mild laxative together with an intestinal antiseptic, such as salol, benzonaphthol, etc.

For the relief of primary infectious myositis a great number of local and general measures have been recommended. In the form characterized by a tendency to suppuration, Brunon advises a treatment which varies according to the particular case. In the hyperacute cases he limits his efforts to the attempt to maintain the patient's strength by means of stimulants and alcohol. In the less acute form he administers preparations of cinchona, and gives exit to the pus as soon as it has formed. In the mild form he has recourse to local counter-irritation or to mercurial inunctions, either alone or accompanied by the application of compresses wet in a carbolic solution after the method practised by Scriba of Tokio.

In the non-suppurative variety, that which I have specially designated by the name of polymyositis, wet cups or flying blisters have been applied; moist compresses have been employed; antiseptic baths and hot douches have been used; and finally the whole list of antipyretics (salicylate of sodium, salol, naphthol, etc.) and of tonics (cinchona, etc.) have been administered internally.

In my opinion, we ought always in the case of an infectious disease to have two indications present to our minds, viz., (1) to strengthen the organism and so increase its resisting powers, and (2) to endeavor to neutralize the action of the micro-organisms and of their toxins by means of antiseptics. I would therefore administer to a patient suffering from infectious myositis, whatever its form might be, tonic preparations, at the head of which I would place kola nut. By reason of the caffeine, the tannin, and the kola red which

this drug contains, it is an excellent tonic, acting in a particularly powerful way upon the heart and circulation. In addition I would advise the administration of cinchona and of alcohol in small quantities under the form of some heavy wine. In certain cases I prefer the use of quinine (the hydrochlorate) to that of cinchona. From the beginning the patient should be kept on a milk diet which will maintain the strength and, by reason of its diuretic action, favor the elimination of the toxins and the waste organic products. The patient should also be allowed to drink as much as he desires of some acidulated beverage, such as lemonade or orangeade.

In the first rank of antiseptic drugs in these cases I would place a soluble naphthol which Stackler and myself have recently introduced under the name of asaprol. This possesses very feeble toxic properties but a marked antiseptic action, and by reason of its ready solubility it is the remedy of choice in all cases when it is desired to act directly upon all the tissues of the organism. It should be given in doses 3 to 4 gm. (45 to 60 grains) a day, either in capsules or in a solution of the strength of 15 grains to each tablespoonful. The solution may be flavored with syrup of bitter orange peel or with a little anisette. Asaprol possesses the great advantages, to mention only these, that it does not diminish the secretion of urine and is so feebly toxic that it can be administered for a considerable period of time without inconvenience.

A measure which I would also recommend is the warm bath, or, when this cannot be given, sponging with warm water to which is added some aromatic alcohol. There are of course other indications to be met in the treatment of this affection. Locally we may employ mild counter-irritation and antiphlogistic measures; and when an abscess is present it should be opened as soon as possible and then treated antiseptically.

In following out the principles above enumerated we shall be in the best position for conducting our infected patients to a state of health. Nevertheless we shall often see our therapeutic efforts come to naught, the disease remaining beyond the resources of our art.

Secondary Myositis.

The muscles may become inflamed in consequence of a large number of influences acting upon them from without. In the first place an inflammation which is primarily limited to a certain region, to one tissue or one organ, may advance slowly and gradually involve the neighboring muscles, giving rise to what has been called "myositis by propagation." The best example that I can give of this form of

myositis is the inflammation which is developed in a muscle in close relation with an inflamed articulation. It is a common observation in cases of arthritis to see, simultaneously with the joint affection, painful symptoms limited to the group of muscles in close proximity to the affected articulation. Examination also shows a certain degree of induration in the affected muscle, and, in the course of time a more or less pronounced atrophy resulting from the long-continued chronic inflammation.

The inflammatory process may travel from any focus whatever and invade the neighboring muscular tissue. In very many cases of secondary myositis more even than in the primary disease the symptoms are often masked by those of the more important disease and thus pass unperceived.

Alongside of myositis by propagation we may mention a "toxic myositis." We are still very much in the dark as to the inflammatory action that poisons are capable of exciting in muscular tissue. I refer here, of course, to mineral or vegetable poisons, leaving out of consideration the microbial poisons or toxins, upon which we possess as yet but few data. These toxic substances certainly exert an injurious action upon the muscles, but this is chiefly of a trophic nature, and its consideration must be reserved for a later section. We might mention here only the acute steatosis, referred to by Hayem, which occurs in the muscles under the influence of poisoning by phosphorus, although, strictly speaking, there is no inflammatory process here present. Cornil has noted the occurrence of the lesions of diffuse myositis in a case of poisoning by ammonia.

As one may see, our knowledge of this subject is still very incomplete, and we must rely upon time to fill up the parts that are wanting. We know much more of the form of secondary myositis of which I now propose to speak, in which the muscular lesions are produced in the course of an acute or chronic general disease. This variety of muscular disease I would call

Symptomatic Myositis.

When we consider the importance of the muscular tissue in the organism, we may well imagine *a priori* that every general disease ought to affect it more or less; and in fact lesions of the muscles have been observed in a very large number of general diseases. Often, however, these lesions are overshadowed or even remain without any external sign of their existence, whence it results that the study of these forms of myositis belongs almost exclusively to the domain of pathological anatomy.

I shall divide the study of symptomatic myositis into four sec-

tions. In the first we shall study the muscular inflammation caused by fevers and infectious disease properly so called; in a second we shall consider rheumatism of the muscles; in a third syphilis, and in a fourth tuberculosis.

The type of symptomatic myositis occurring in fevers is furnished by the myositis complicating typhoid fever. It is to Zenker and Waldeyer that we are indebted for our first knowledge of this variety of muscular inflammation. Hayem has completed the work of these authors and has directed special attention in a number of interesting articles to the subject of secondary infectious myositis. The occurrence of myositis has been noted in typhoid fever, small-pox, scarlatina, measles, erysipelas, diphtheria, pernicious jaundice, infectious endocarditis, and glanders. We may indeed assert that all infections diseases, whether the micro-organism be already recognized and isolated or whether its presence be only suspected, may lead to muscular inflammation. In this category I do not hesitate to include influenza, although we have as yet no anatomical proofs establishing a connection of this sort. I find my justification for this inclusion in a case observed by me during the epidemic of 1889–90. A young man of twenty-one years, without any constitutional taint, was attacked by the grippe and presented symptoms of broncho-pneumonia and of gastro-intestinal disturbance. The patient had a rather long period of convalescence, but he finally recovered and by the end of two months his attack was nothing more than a memory. At this time, while mounting a horse he suddenly, without being conscious of having made any special effort, felt a sharp pain in the upper and anterior part of the left thigh. He was unable to continue riding and could not even return to his home on foot. Upon examination a very severe pain was found localized in the adductors, and in the course of the following days an ecchymosis of the skin covering this portion appeared and confirmed the diagnosis which had been already made of rupture of the muscle. I am convinced that this rupture had been made possible by a myositis due to the action of the grippal infection.

Hayem, in the work above referred to, gives the following table:

Myositis occurred	22	times in	24	cases of	small-pox.
"	19	"	21	"	typhoid fever.
"	1	time in	1	case of	scarlet fever.
"	2	times in	3	cases of	measles.
"	3	"	3	"	acute generalized tuberculosis.
"	1	time in	2	"	pernicious jaundice.
"	1	"	1	case of	wandering erysipelas.
"	1	"	1	"	puerperal fever.
"	1	"	2	cases of	tubercular meningitis.

Among all infectious diseases two are of special importance from the point of view that now concerns us, viz., typhoid fever and small-pox, to which I would add measles, a disease which was the probable cause of a sclerosing myositis in a case recently reported by Gaucher and Marage.

Pathological Anatomy.—At the autopsy the muscles are found swollen and rigid; their color may vary from a dark red to brownish; in their substance are seen points of rupture of the fibres and small hemorrhagic or purulent foci.

Hayem describes three degrees of symptomatic myositis. In the first degree the lesions are not very clearly marked; the muscles are indurated and swollen, and their color is darker than normal. Under the microscope the muscular fibres present a granular or sometimes waxy appearance, and there is seen to be a beginning increase in the nuclei of the muscular cells and of the internal perimysium.

In the second degree the muscular tissue is seen to be paler; certain of the bundles are of a grayish-pink color, others are yellowish or whitish. There is also an extravasation of blood, and the tissue becomes very brittle. Under the microscope we find the lesions of the first form in a more advanced state; the altered fibres are broken, the nuclei are much increased in number, and we recognize the lesions of granular and waxy degeneration. Fatty granules are found especially in the granular degenerated fibres; the waxy fibres are broken into larger masses.

In the third degree we find ruptures of the muscular tissue and extensive effusions of blood or even purulent collections. The muscle is very soft and friable, its color is yellowish, grayish, or brownish, and the fibres are separated. But alongside of this destructive process proceeds one of repair which is very interesting to observe. There is a true regeneration of the muscular tissue starting from the nuclei of the muscles and also from those of the internal perimysium.

There are three points of particular importance in the pathological anatomy of this form of myositis, viz., the work of regeneration, of which I have just spoken, and the granular and waxy degenerations. We know that granular degeneration is characterized by a deposit of fine granules in the substance of the primary fibres. The vitreous degeneration, which is called waxy by Zenker, consists in a tumefaction of the primary fibre, the muscular elements of which have become transformed in mass into a substance having a shining aspect.

In typhoid fever we meet especially with waxy degeneration, and in small-pox with granular degeneration.

Etiology.—As regards the pathogenesis of these inflammations, the increased temperature due to the fever was formerly looked upon

as a factor of the greatest importance. While not denying wholly the influence of this cause, I believe that there is another factor of much greater importance. Here again we have to consider the action of microbes. In a lecture on typhoid fever recently published, Achard has expressed himself as follows: "These forms of myositis associated with typhoid fever are produced by micro-organisms, and in our case we were able to detect Eberth's bacillus together with the staphylococcus albus in the fluid withdrawn by aspiration." It can therefore not be doubted that the micro-organisms are the essential factors in the production of the muscular inflammations occurring in the course of acute infectious diseases.

The *symptomatology* of these forms of myositis is often obscure, and in many cases there is nothing to lead us to suspect the condition which is revealed at the autopsy. Nevertheless the fatigue and feeling of lassitude, which are among the first symptoms of an infectious fever, must certainly be due to inflammation of the muscular tissue. This depression, a feeling as though the limbs were broken, and vague pains referred to the muscles are present more especially in typhoid fever, small-pox, and influenza. I do not, however, believe that we ought to refer the intense rachialgia which accompanies the onset of small-pox to a myositis affecting the dorsal and lumbar muscles. That is rather, in my opinion, a phenomenon referable to the spinal nerve centres, the rapidity of its appearance and its immediate intensity arguing against the supposition that it is of muscular origin.

But in addition to these indefinite symptoms, which may easily be confounded with those of the original malady, we find others more precise. Small-pox and especially typhoid fever furnish us with examples of this kind. We find certain muscles or groups of muscles more painful than others, and it is especially the recti abdominis, the pectorals, the adductors, and the muscles of the extremities that are chiefly affected. Their contraction causes pain, and palpation enables us to map out the inflammatory induration of which they are the seat.

The most frequent complication of myositis is muscular hemorrhage, which is not infrequently observed in typhoid fever. It is this fact, indeed, which has drawn the attention of clinicians to the muscular lesions occurring in the course of this affection; and for a considerable time the only recognized form of symptomatic myositis was that complicating typhoid fever. The muscular hemorrhage takes place during the third or fourth week of the disease, and is the result of the rupture of the muscular fibres which occurs during contraction. It is for this reason that the hemorrhage is most commonly

observed in the rectus abdominis muscle, which is the one that enters into action whenever the patient turns in bed or attempts to sit up.

When hemorrhage has taken place we find a painful tumefaction at the site of the lesion, which is indurated, somewhat elastic, and occasionally fluctuating. In the course of a few days an ecchymosis appears under the skin; this may gradually become absorbed, presenting all the colors indicative of this process, or may become the seat of suppuration. In the latter case the skin becomes red and hot, there may be some fever, and all the signs point to the presence of pus, which should immediately be evacuated.

In the category of muscular inflammations which we are now considering I would range that described by Gaucher and Marage under the name of the myositis of measles. The case reported by these authors was that of a child seven years of age who presented symptoms of a chronic myositis in the right calf and torticollis affecting the sterno-cleido-mastoid muscle of the left side, consequent upon an attack of measles.

The forms of secondary myositis which we have just been studying exert a very feeble influence upon the progress of the disease which gives rise to them. Nevertheless if suppuration occurs we have a complication that may be of serious import by reason of the depressed condition of the organism already weakened through the action of the primary disease, and which may retard recovery even if it leads to nothing more grave.

Treatment.—There is almost nothing to add here to what I have said in the corresponding section under the heading of primary myositis. At the beginning we may combat the inflammation of the muscles by means of mild revulsives. If a rupture has occurred and been followed by hemorrhage, immobilization of the part or light compression will usually bring about resorption of the effused blood; only occasionally will it be necessary to make an incision into the muscle. If pus forms we must evacuate it and treat the wound antiseptically. In the chronic sclerosing form we must have recourse to inunctions with Neapolitan ointment, electricity, and methodical massage.

Rheumatic Myositis.

I remarked above, when speaking of acute primary myositis, that certain authors regarded this as belonging to the class of rheumatic diseases. Indeed we are always tempted to refer muscular inflammations to the agency of the rheumatic poison. I believe, however, that there is an independent acute primary myositis, such as has been described above, and that apart from this there is a rheumatic

myositis such as we shall now study. Inflammations of this character affect both sexes and all ages, and accompany or alternate with other manifestations of the disease. This fact and that of heredity are the main points upon which we may base a diagnosis.

Rheumatic myositis may be acute, subacute, or chronic. Changes of temperature play an important part in the etiology of the individual attacks, and we thus find them of more frequent occurrence during warm weather. At this time the skin is more active, and one is more exposed to sudden chills from checking of the perspiration. Overwork and fatigue are also to be classed among the etiological factors.

The pathological anatomy of rheumatic myositis is not well understood. The occasion for making an autopsy on a subject of this disease seldom presents itself, and it has been disputed that there are any material lesions of the muscle. However, Hayem has examined the muscles of several persons who have died during the course of acute articular rheumatism, and has found the muscular fibres rigid, swollen, and slightly granular. Other observers have stated that waxy degeneration was present. Suppuration does not ordinarily occur in this form of myositis, though it might exceptionally take place. The most important lesion occurring in rheumatic myositis is atrophy of the muscle or muscles affected.

Symptoms.—The acute form of rheumatic myositis is accompanied by very severe pains which the slightest movement excites. Occasionally, though rarely, there is an elevation of temperature of short duration. The affected muscle may be in a state of contraction. Usually the inflammation involves but few muscles. The best examples of rheumatic myositis which I can cite are the inflammation of the sterno-cleido-mastoid, otherwise known as torticollis, and that of the dorso-lumbar mass which goes under the name of lumbago.

Chronic rheumatic myositis is a very common affection, and we may say that the great majority of cases of chronic myositis not following the acute form are of rheumatic origin. In this case we find the muscles more or less indurated and often shortened. The pain is not so severe as in the acute form, but it nevertheless constitutes an important symptom. The patients suffer from movements, and furthermore pain is excited, as in other rheumatic conditions, by various meteorological changes, such as a lowering of the temperature of the atmosphere, variations in barometric pressure, changes of electrical tension, etc.

The diagnosis of rheumatic myositis involves a consideration of two points: (1) Have we to do with an affection of the muscles; and (2) is it of rheumatic nature? We can satisfy ourselves as to whether

the muscles are affected by means of careful palpation of the parts, mapping out exactly the limits of the painful region; in this way we may easily exclude other causes of suffering, such as neuralgia, by observing that the pain is felt in greatest intensity in the body of the muscle and at its points of insertion, and not along the course of one of the main nerve trunks. In regard to the second point we must base our opinion upon the hereditary and personal antecedents of the patient. We should remember also that the temperature in rheumatic myositis, even in the most acute forms, is seldom elevated to any great extent, and that suppuration is an absolute rarity.

The prognosis is in general favorable; nevertheless we should not forget that chronic myositis may persist for a very long time and may be the cause of atrophy of the muscle.

Treatment.—In acute cases we should have recourse to revulsives and to analgesic and antiseptic remedies, such as salicylate of sodium and asaprol. Quinine and antipyrin may also be of service.

In chronic rheumatic myositis there are three therapeutic measures which may give good results, viz., hydrotherapy, electricity, and massage; these may in special cases be employed alternately or in combination.

Among the hydrotherapeutic measures which we may prescribe are vapor baths, very hot turpentine or sulphur baths, and hot douches. The patient may with advantage be sent to some watering-place suitable for the treatment of these cases. Among these places I would class in the first rank Néris and Aix-les-Bains. In the latter station massage of the affected muscles, well carried out under the douche, gives excellent results.

In addition to hydrotherapy we have mentioned massage and electricity. The former applied at the proper time is often an efficacious means of combating the atrophy. As regards electricity, some writers, among others Weissflog and Danion, express a preference for the faradic current, while others (Erb and Remak) recommend the continuous current; others again (Larat and Vogt) regard the action of sparks from the static machine as the most efficacious in the treatment of chronic rheumatic myositis.

Doumer claims to have derived great advantage from the employment of franklinism under the form of effluvation. He attaches no importance to the mode of application, whether on the uncovered skin or through the clothing, and says that equally good results are obtained whether the parts are naked or covered, although the sensations of the patient differ somewhat in the two cases. When effluvation is practised on exposed parts the patient feels a sensation as of a fresh current of air, while when the parts are covered he feels a

little pricking and formication. In either case there is a sensation of heat in the parts and very soon the pain disappears or is greatly diminished. A few sittings are usually sufficient to bring about this favorable result. My own preference in the treatment of chronic rheumatic myositis is franklinism, either sparks or the effluvation practised in the way recommended by Doumer.

Surgical procedures may be required for the relief of the shortening of a muscle that may take place in chronic myositis. In the case of torticollis, for example, we may be able by means of tenotomy to reduce the deformity caused by the contracture of the sterno-cleido-mastoid muscle.

Syphilitic Myositis.

Syphilis may produce lesions of a peculiar kind in muscular tissue. These were for a long time unrecognized, but their occurrence is now admitted by all writers on the subject. The works of Ricord, Notta, Lagneau, Gosselin, Maurice, and recently Prost (Thèse de Paris, 1891) have shown in a very clear manner the part that syphilis plays in the pathology of the muscular tissue. All the muscles are not attacked indifferently, those of the right side being more frequently invaded than those of the left, and those suffering the most which have the most labor to perform. Among these may be mentioned especially the masseter, the sterno-cleido-mastoid, the biceps, and the flexor muscles in general. The extensors are rarely the seat of syphilitic myositis, three cases only in which the triceps brachialis was affected having been reported. In most of the recorded cases it was the biceps that was attacked.

The disease may appear during any of the stages of syphilis, but is most commonly a manifestation of the secondary period, and is frequently accompanied by the eruptions peculiar to this period. Rheumatism and gout have been invoked together with syphilis in the etiology of the inflammation. It has been said that while syphilis played the principal rôle in the causation of the disease, the morbid phenomena were manifested by preference in a soil previously prepared by rheumatism or gout. Without wishing to deny wholly the influence of these diatheses, I must confess that the syphilitic infection appears to me to be the chief if not the exclusive etiological factor.

The following is what generally takes place: A patient presents himself with the forearm flexed upon the arm, and affirms that he is unable to execute the slightest movement of extension. Examination shows the biceps in a state of contracture and attempts to make forcible extension are fruitless and only excite severe pain. The skin presents no evidence of inflammatory action beneath, the color being

normal and no heat being perceptible in the part. Careful palpation shows that the biceps alone is affected, its tendon forming a tense prominence like a cord. To judge from the prominence of the belly of the muscle and from its shortening, it might be thought that it was in a state of contraction, but there is not the normal consistency of a muscle in a state of active contraction; it is less hard than a healthy muscle should be. It is smooth, presenting no knobs or bosses on its surface. Strong palpation with the tip of the finger causes pain at the bend of the elbow, at a point on the inner side of the biceps tendon. As already remarked, most intense pain is caused by attempts at extension of the arm, and these attempts are moreover utterly fruitless, the movements of the elbow being extremely limited. We are therefore in the presence of a patient with contracture of the biceps, but we may have difficulty in discovering the cause for the contracture. The patient states that this condition did not come suddenly, but had been growing gradually more marked for some days. At first there was merely some difficulty in moving the arm on account of a certain stiffness in the elbow, and then it was found that the forearm could not be fully extended. This at first did not cause much inconvenience, but little by little the arm became bent and stiff. The patient will frequently be seen to be very nervous, and the first thought often is that the case is one of hysteria; but the sensibility of the skin is found to be perfectly normal. Another supposition is that there is some lesion of the central nervous system; but examination shows no alteration in the reflexes. Further examination will reveal the fact, either in answer to close questioning or through the discovery of the characteristic lesions of the skin or mucous membranes, that the patient is suffering from syphilis. In this particular instance careful examination of the affected region will show that it is the muscle that is diseased and not the osseous or articular structures.

In the case which I have just sketched I have had in view syphilitic myositis of the biceps, which was chosen as the type of these affections because it is the one most commonly encountered. The symptoms will vary a little, of course, with the region involved, but taking into consideration the difference in location there will be little difficulty in arriving at a diagnosis.

Although pathological investigations of this condition are wanting I am convinced that the lesion is a myositis. According to Virchow, we have to do with an interstitial myositis due to a colloid degeneration of the muscular tissue. A new growth of connective tissue takes place, he holds, between the muscular fibres, leading to their atrophy and eventual destruction.

Syphilitic myositis is a benign affection, hence we may readily understand why the study of its pathological anatomy is incomplete. Indeed this form of myositis is readily curable under appropriate treatment. Its duration is often rather long, it being a question not of days but rather of weeks or months. Three months has been given as the average duration.

Treatment.—This is a question of the first importance in dealing with syphilitic myositis. Counter-irritation is here of not the slightest benefit, and the entire subject of local treatment may well be left out of consideration. If the pain is very severe we may combat it by means of soothing local applications, but as a rule it is the general treatment that demands our special attention.

The two great remedies for syphilis are always mercury and iodide of potassium. We are constantly bringing out more and more clearly the special indications for the employment of one or the other of these remedies either alone or in combination; and experience has shown that the iodide often is more efficacious, even at an early period of syphilis, than the mercurial preparations. Syphilitic myositis, which belongs more especially, as we have seen, to the secondary stage of the disease, is efficaciously combated by iodide of potassium. Fournier has very justly insisted upon this point; and he says that he has had the best results with small doses of the iodide. I am entirely in accord with him in this opinion, and regard the iodide of potassium in small doses as a true specific in syphilitic myositis.

Tubercular Myositis.

Passing over the loss of muscular tissue which takes place in tuberculous subjects in proportion as the disease progresses, a loss the study of which belongs more properly to the section of trophic disturbances, we may consider for a moment the inflammatory processes of which I believe the muscles are often the seat in persons suffering from tuberculosis. We very frequently, in fact, hear phthisical patients complain of pains in the extremities, especially in the legs. While not forgetting the algetic symptoms referable to cachetic phlebitis, it seems to me that we are justified in regarding some of these painful sensations as of muscular origin. If we palpate carefully the muscles of the legs, more especially those of the calves, we shall find that pressure excites more or less pain which I believe is due to the presence of myositis.

In addition to this form, which I may call latent, in which the symptoms are rather vague and indefinite, there is a tubercular myositis characterized by unmistakable signs. Delorme and Reverdin

made an important contribution to the literature of tubercular myositis in a paper read by them before the French Surgical Congress in 1891. Although this affection, and particularly its treatment, belongs rather to the domain of surgery, I cannot omit all mention of it in a treatise on diseases of the muscles. The patients are usually young and often in apparent health. Delorme had observed the disease in young people whose appearance would never suggest that they were the subjects of bacillary infection. This author reported a case of tubercular myositis affecting the pectoralis major muscle, in which he noticed a swelling the size of a small hen's egg in the body of the muscle. The skin covering it was of a purplish color. There was no fever present. Upon incision the great pectoral was found to be almost completely invaded by a soft mass unmixed with pus or extravasated blood. A diagnosis was withheld and even the microscopical examination did not remove the doubt as to the true nature of the disease. It was evident that myositis was present, but there was nothing to establish its tubercular nature. The course of the disease, however, left no doubt as to its character, for the patient soon began to cough, he became emaciated and presented all the symptoms of a tubercular phthisis, and the autopsy confirmed the diagnosis made *intra vitam*.

Delorme reports three other cases of sclerosing tubercular myositis, and he draws particular attention to the difference existing between this and the suppurating form of tubercular inflammation of the muscular tissue. In the latter disease there is simply a cold abscess formed in the substance of the muscle, either occurring idiopathically or following tubercular disease in the osseous or articular structures.

The only local treatment that is indicated in these cases is operative, but before undertaking this we must consider the general condition of the patient. As in all other forms of tuberculosis, our efforts should be directed toward putting the patient in the best possible state to resist the bacillary invasion. He should live under the most favorable hygienic surroundings, have a plentiful allowance of nutritious food, and be fortified by appropriate tonics for his struggle against the invading bacteria.

As to the prognosis, it is easy to comprehend its gravity, I was going to say its fatality.

Trophic Affections.

I confess to a certain feeling of hesitation in entering upon the study of the trophic affections of the muscles, for I am convinced

that many of the questions here to be discussed will be modified in the future and that later studies will throw a new light upon them. However, we can but recite the facts as they appear to us at the present moment.

This section, like the preceding one, may be conveniently divided into two parts, the first being devoted to a consideration of primary trophic disturbances of the muscular tissue, and the second to those arising in the course of, and dependent upon, other diseases.

Primary Trophic Affections.

It is especially to this class of primary trophic troubles that the remarks just made apply. In this group we have a whole series of facts in which the muscular lesion constitutes or seems to constitute the entire disease, and at the autopsies made upon subjects of these affections it has been impossible to discover any lesion whatever of the central or peripheral nervous system. The only alteration discovered has been the disappearance of the muscular tissue, and on the strength of these findings the type of primary myopathies has been established. We cannot here enter upon the path of hypotheses, and must confine ourselves to a study of the facts disclosed by anatomical investigations. However, some of the characteristics presented by the primary myopathies which we shall now proceed to study are of such a character as to lead us to believe that the last word has not yet been said. Of course, negative observations are of value, especially when made by competent observers, yet pathological anatomy, and especially histology, has doubtless many surprises in store for us, and it need cause no astonishment if these primary myopathies should eventually be shown to belong properly to the class of nervous affections. Until better informed, however, we must continue to group them among the muscular diseases.

Primary Progressive Myopathy.

This affection did not enter already complete into nosological nomenclature, but took ground there little by little, being built up by the approximation of elements at first regarded as in no way related to each other. Its history is therefore somewhat complex and has only recently been definitely established. At first the two forms of primary myopathy which we shall study, namely, the atrophic and the pseudo-hypertrophic, were regarded as entirely distinct one from the other. This separation was of necessity made at the beginning, for authors could not dream of classing together two affections which

objectively were so different. As we shall see later there is on one side a considerable increase in the volume of the muscles—an apparent increase, it is true, since the hypertrophy is really caused by a proliferation of the adipose tissue—and on the other side a true atrophy, a diminution of volume of the muscular tissue proper. It was very natural, therefore, to describe one disease as an hypertrophy with diminution in power, and the other as an atrophy; and it was only later that a closer examination of the conditions present allowed of the two affections apparently so dissimilar being brought under one heading.

To Duchenne of Boulogne we owe the first description of the disease in question. As early as 1861 this author described an hypertrophic paraplegia of infancy. Its pathogenesis at that time was not well understood, as the affection was referred to a cerebral lesion, but its symptomatology was clearly established. In 1866 Cohnheim and Eulenburg, basing their opinion upon the pathological anatomy of the disease, denied that it was due to any cerebral lesion, and placed it among the purely muscular affections. In another work on Pseudo-hypertrophic Paralysis, published in 1868, Duchenne also recognized the non-participation of the nervous system. In 1871 Charcot likewise stated that he had found in this disease lesions of the muscular tissue only.

Primary myopathic atrophy was, as I have said, for a long time confounded with the other muscular atrophies. Even after the works of Duchenne (1849) and Aran (1850) there was little settled as to the nature of muscular atrophies. Many regarded them all as primary, and it was only later, thanks especially to the labors of Luys, Hayem, Vulpian, and Charcot, that we came to appreciate the important part played by the nervous system in many of these affections. But we do not mean by that to assert that all the progressive muscular atrophies should be regarded as of nervous origin. Leyden insists that there is a type of atrophy of purely myopathic origin, and he has described an hereditary form of progressive muscular atrophy. In this form the atrophy begins in the lower extremities and does not involve the upper. Möbius, in 1879, endeavored to bring out the points of relationship between the disease described by Leyden and pseudo-hypertrophic paralysis, and this was the first attempt to bring these two forms closer together. Zimmerlin noted a type in which the atrophy was especially marked in the upper portion of the body, the lower extremities not being attacked until much later. Eichhorst published a case in which the trouble began in the perineo-tibial region. Then in 1882 and 1884 Erb studied a scapulo-humeral form of what he called juvenile progressive muscu-

lar atrophy, and in his last work he insisted upon the identity of all primary myopathies.

In 1885 Landouzy and Déjerine, who had already the year previous presented to the Académie des Sciences a note on myopathic atrophies, endeavored to establish the facio-scapulo-humeral type, and to distinguish it from the juvenile form of Erb. It is to the last-named author that we owe the most recent treatise on this subject. In 1891, having collected and studied all the different cases of atrophy, simple or pseudo-hypertrophic, he marked off sharply the disease to which he gave the name of progressive muscular dystrophy. He demonstrated by microscopical studies that the lesions were always the same whether there was hypertrophy or not, that the evolution was in all cases identical, and that the apparent increase in size depended entirely upon the greater or less quantity of fat in the sclerotic tissue which had replaced the atrophied muscle.

I have already said that it has been impossible to discover any nervous lesions in any one of these forms constituting this nosological ensemble. We shall see, however, that there is an affection known under the name of muscular atrophy of the type Charcot-Marie which resembles in several of its characteristics the myopathic atrophies, but which presents at the autopsy true nervous lesions. This has been regarded by some as an intermediate form between the two classes of atrophy. Perhaps in the course of time we shall be able to refer the myopathic conditions now called essential to some trouble of the nervous system.

It is then, as we have just seen, by a succession of works in no way related to each other that we have arrived at the constitution of a group of primary myopathies. Although it is definitely established now that pseudo-hypertrophic paralysis, as described by Duchenne, and progressive atrophic myopathy constitute but one and the same morbid entity, yet we shall find it more convenient for the sake of clearness of exposition to devote a chapter to each of these clinical varieties.

Pseudo-hypertrophic Muscular Paralysis.

This disease belongs to childhood, and rarely begins after the tenth year, although cases have been reported in children of fourteen or fifteen years. It occurs more frequently in boys than girls, and often attacks several members of the same family.

The direct examination of the diseased muscles during life has been made by removing small portions by means of the harpoon. This examination has enabled us to see that the hypertrophy is only apparent and that the increase in volume of the muscular prominences

is due solely to an increase in fatty tissue. Under the microscope it is seen that the muscular fibre has almost entirely disappeared. At the same time there is an accumulation of adipose cells to such an extent that little by little the fatty tissue replaces the muscular. The more or less vivid red color of normal muscular tissue has disappeared and given place to a pinkish-yellow hue.

Alongside of the pseudo-hypertrophied muscles it is often possible to find others which are decreased in size—simply atrophied. The tendons never take part in the pseudo-hypertrophic process. Examination of the nervous centres gives negative results, and, notwithstanding the observations published by Babes, in which the intramuscular nerves seemed to present some alterations, it is generally admitted to-day that the muscular lesions constitute the entire disease.

Symptoms.—There are two things which attract attention and excite a suspicion of pseudo-hypertrophic paralysis, viz., an increase in volume of certain groups of muscles and a weakness which seems to increase in proportion to the progress of the apparent hypertrophy. At the beginning of the disease it is the lower extremities which are attacked, and what first attracts attention usually is the prominence of the calf muscles. The muscles of the thigh and gluteal region become involved in the same process, and the glutei, the sacro-lumbar muscles, the flexors and adductors of the thighs are seen to stand out prominently. In the same way the quadratus lumborum, the deltoid, the serratus magnus, the periscapular muscles and those of the arm are invaded. Frequently these muscular groups atrophy instead of becoming hypertrophied. But the most salient feature of the picture is the excessive volume of the lower extremities, and, in interesting contrast to this, a gradually increasing weakness involving these same regions. At the commencement of the affection this weakness is not very pronounced. It is only remarked that the child stands less firmly on his legs and often falls. As the lesion progresses and the muscular tissue gives place to fat, walking becomes more and more difficult. In order not to fall the patient separates his legs, and in walking he bends backward and inclines his body to one and the other side; in a word, he waddles like a duck. This expresses very accurately the manner of progression of a child with pseudo-hypertrophic muscular paralysis. After sitting or lying the patient experiences the greatest difficulty in raising himself to an erect posture, and he is forced to execute a series of movements in order to supplement the insufficiency of his thigh and leg muscles. The first thing that he does is to place himself on his belly; then with his hands he rolls himself together and rises with difficulty, supporting himself with his hands resting successively on different seg-

ments of the lower extremities. It has been said very aptly that the patient climbs up himself.

Palpation of the affected parts gives the peculiar sensation of softness inherent in fatty tissue, which is very different from that of normal muscular tissue.

Pseudo-hypertrophic muscular paralysis invades gradually more and more of the muscles. After having halted for some time in the lower extremities it attacks most of the other muscles of the body, this time often under the atrophic form. The atrophy may also follow upon the false hypertrophy. The feet are sometimes deformed, being drawn into the equinus position. The face may likewise become involved, as has been noted by Duchenne, Weir Mitchell, and others. The patient then presents the phenomenon of a gaping mouth, and his atrophied muscles prevent the complete closure of his eyelids.

All these symptoms develop gently without commotion. There is no fever, the patient does not complain of pain, and nothing is present to give warning of the gravity of the affection. Duchenne in his first memoir drew attention to the fact that children suffering from this disease often give evidence of a weakened intellect, and as we have seen he was even led to regard pseudo-hypertrophic paralysis as dependent upon a cerebral affection.

All the other organs perform their functions well, and for a long time the patient presents every appearance of perfect health. Occasionally the progress of the disease seems to be arrested for a time, but usually its march is resistless and sooner or later the child is condemned to absolute immobility. The atrophic process goes steadily on, and generally the patients succumb to some intercurrent disease the seat of which is most commonly in the lungs. Thus tuberculosis or broncho-pneumonia frequently terminates the pseudo-hypertrophic paralysis. The disease reaches its greatest development in from ten to eighteen years, and the sufferers seldom live beyond their twentieth year.

Diagnosis.—It would be hardly possible, given the symptomatology and course of the disease which we have just considered, to confound pseudo-hypertrophic paralysis with any other disease. I ought to note that there are cases of an atrophic nature from the commencement; but, as I have already said, I separated the essential hypertrophic myopathies from the atrophic affections solely as a matter of convenience in clinical descriptions. As a matter of fact these two forms frequently coincide and are confounded with each other, and the important point in a diagnostic sense is to establish the primary myopathic nature of the affection. Once this point is

settled we may class the case according to its most prominent features among the pseudo-hypertrophies or among the atrophic forms which we shall study in a subsequent section.

We must not confound pseudo-hypertrophic myopathy with infantile paralysis, paraplegia, or progressive muscular atrophy. This may easily be avoided by a study of the previous history and by carefully noting the progress of the disease from its inception. The apparent hypertrophy with diminution of strength is a very characteristic feature. Thomsen's disease is sometimes accompanied by an increase in size of the members, but it presents in addition a most characteristic symptom, viz., the rigidity which is manifested at every attempt at voluntary movement and which relaxes gradually, permitting of the movement being made in a normal manner.

Treatment.—After what has been said concerning the prognosis of this affection we may conclude that there is little to be hoped for from treatment. It ought none the less, however, to be instituted at the earliest possible moment. The administration of tonics is indicated, the special form being varied from time to time. We may give in succession cod-liver oil, cinchona, phosphate of lime, and arsenic. The child should live under the best hygienic conditions, and may with advantage be sent to the seashore. But the point to be most strongly insisted upon is electricity. Faradization has seemed to give some good results in these cases. It will be necessary to continue its employment for a very long time, for years even, care being taken, however, to discontinue the applications for a few weeks at a time at intervals of three or four months. Ladame of Geneva has proposed a form of electrical massage by means of galvano-faradization, but this procedure, which combines the employment of faradic and of galvanic electricity, must be carried out with great caution, for it is very powerful in its effects and might give rise to injurious consequences. It ought also to be applied only by physicians who are thoroughly skilled in the practical application of medical electricity.

Progressive Atrophic Myopathy.

For the sake of clearness of presentation I have thought it best to describe separately the two forms of primary myopathy, viz., pseudo-hypertrophic and atrophic paralysis, notwithstanding that these two clinical types are of the same nature. We will now take up the consideration of the simple atrophic form.

In speaking in a general way of the history of primary myopathies, I have sufficiently indicated in what way the nosological type which we are now considering came to be established. We have seen

Leyden, Erb, Landouzy, and Déjerine bring important contributions to this subject, the final analysis of which was made by Erb in 1891.

As in the case of pseudo-hypertrophic paralysis, we have here only the vaguest etiological data. All that we know is that this affection is rare, that it attacks in equal proportion the two sexes, and that it appears usually in later childhood, although it may be developed at any age. Joffroy and Achard have indeed reported a case of this disease occurring in a woman fifty-five years of age. Fatigue and physical overwork have been alleged as factors in the production of the affection, and the possible influence of infectious diseases has also been mentioned. Thus measles and scarlatina have been accused as predisposing to the paralysis, but the only point of real interest in the etiological study of the affection is heredity. It is not rare to see several members of the same family affected with muscular atrophy. Eichhorst, Landouzy, and Déjerine have insisted particularly upon morbid heredity, and they report several instances in which the number of cases of this affection have gone on increasing from generation to generation, the early mortality of the other children also increasing so that in a short time the entire family of myopathics would become extinct. We find numerous well-attested facts that show that one or more of the children of a myopathic are liable to be subjects of the same disease in one or other of its forms.

Pathological anatomy sustains the view that there is a primary form of myopathy, for the nervous system presents no changes whatever, and the only lesions found are those of the muscular tissue. This is the seat of a more or less marked atrophy localized in one or another region according to the variety of the disease with which we have to do. The color of the affected muscles is reduced in intensity. Histological examination confirms what is learned by simple inspection, the fact, namely, of a progressive destruction of the muscular fibre.

As I have before remarked, progressive muscular atrophy presents several different types which it is possible to describe separately. Thus we have the scapulo-humeral (Erb), the facio-scapulo-humeral (Landouzy and Déjerine), the Leyden-Möbius, the Zimmerlin, the femoro-tibial (Eichhorst), and the femoral with claw-like retraction of the toes (Brossard).

The scapulo-humeral type described by Erb in 1882 begins during childhood or at puberty, the atrophy showing itself first in the muscles of the shoulder and in those of the arm. The muscles of the back, lumbar region, and lower extremities may also participate in the paralysis, and this early in the course of the disease, but usually they are not attacked until much later. The lesions are most commonly sym-

metrical, although Erb has seen them invade one side first, the other side not participating until after a considerable period. As long as a sufficient quantity of muscular tissue remains the reflexes are preserved. There are no fibrillary contractions, and the electrical contractility remains normal, showing only a diminished intensity which becomes more and more apparent in proportion as the muscular tissue disappears. According to Erb, the muscles of the face are never attacked in this form of the disease. Affections of this part are, however, occasionally observed and serve as a connecting link between this form and the following which has been more particularly studied by Landouzy and Déjerine.

The facio-scapulo-humeral type belongs in general also to childhood but has been known to develop in adolescence, adult life, and almost in old age. It is characterized by a primary symmetrical atrophy of the muscles of the face (orbicularis, palpebrals, and labials). This atrophy naturally produces a special facies, as a consequence of which the disease may readily be recognized by simple inspection alone. Landouzy and Déjerine have drawn a very accurate picture of the appearance presented by these patients. They have described the gaping hebetudinous air, the immobility of the features, the incomplete closure of the eyes, the half-opened mouth, the projecting lips, and the widening of the buccal opening when laughing, so that the patient is said to laugh "all across his face."

The atrophy may remain for a long time limited to the muscles of the face, and it is usually only after a long period that the muscles of the shoulder and arm are invaded. Later the muscles of the forearm and hand, and finally those of the lower extremity, are seen in turn to become atrophied. The power of sensation persists, and the reflexes and electrical reactions remain as long as there is any muscular tissue.

In *the Leyden-Möbius type*, the atrophy may begin in the muscles of the lower extremity, mounting from the legs to the thighs, the lumbar region, and finally attacking the upper extremities. This form resembles in its course pseudo-hypertrophic paralysis, but it differs from it in that there is less apparent increase in volume of the affected muscles.

The Zimmerlin type includes those cases in which atrophy is most marked in the upper half of the trunk and in the upper extremities, not attacking the lower extremities until later.

The femoro-tibial type of Eichhorst commences with atrophy of the lower extremities, principally of the interossei and the triceps cruris. As the disease advances the lesion invades the lower part of the trunk and finally the scapular region and arms.

The Brossard type resembles the last, but is distinguished from it by the fact that there is retraction *en griffe* of the toes.

Prognosis.—The course of progressive atrophic myopathy is usually very slow, and we may say that the prognosis, at least in those forms in which the atrophy affects chiefly the upper parts of the body, is more favorable, or rather that the end is much further off, than in pseudo-hypertrophic paralysis. Indeed, as long as the lower extremities are not invaded the patients can walk about, take exercise, are not confined to the bed or even the room, and are thus in much better hygienic conditions than those whose legs are paralyzed. It is thus easy to understand that they have a greater resisting power, and we may see persons affected with these forms of myopathy surviving for thirty or forty years or even longer. In atrophic, as in pseudo-hypertrophic, myopathy death usually results from general cachexia, organic disease, or frequently from tuberculosis.

The *diagnosis* of atrophic myopathy will rest not so much on the presence of atrophy as on the peculiar course of the disease. In the most common form, that belonging to the Landouzy-Déjerine type, the atrophy of the muscles of the face, and the peculiar appearance presented by the patient in consequence, will hardly permit of confounding the disease with progressive muscular atrophy or with infantile paralysis. When the disease appears under one of the other forms which I have described, the diagnosis may be more difficult. In the case of those whose lower extremities are first affected, and those presenting the scapulo-humeral type (Erb), there may be some uncertainty. The first may be thought to be suffering from paralysis with atrophy of toxic origin (alcoholic) or from some form of myelitis; the second may suggest atrophy either of myelopathic origin or consecutive to an articular lesion. I have said that the muscles of the face are often affected in this type, and this may be of aid in arriving at a correct diagnosis. In all cases, whatever the form, we may generally make a diagnosis by studying the commencement and course of the disease and noting the absence of fibrillary contractions and of the reaction of degeneration.

As regards *treatment*, I have nothing to add to what has already been said in speaking of pseudo-hypertrophic paralysis.

After having passed in review the symptoms and course of primary myopathies we cannot help calling attention to the fact that there are still many obscure points about the disease. Thus all the organs have been investigated to determine the cause of these symmetrical lesions, and these researches have led to many interesting discoveries. The troubles have been referred among other causes to malformations of the osseous structures. In addition to the antero-

posterior flattening of the thorax noted by Déjerine, to the great frequency of fractures of the long bones to which attention has been called by Halleon, the occurrence of deformity of the cranium in the subjects of myopathy has also been described. Marie especially has studied these cranial deformities. The existence of these malformations, the nervous system being intact, would justify the hypothesis that primary myopathies are hereditary diseases affecting the muscular system; the muscles are, as it were, congenitally deformed; there is something wanting in them, the lack of which gives occasion later to the appearance and development of the disease. The general belief at the present time is that the affection is a purely muscular one, but certain writers, among them Erb and Lépine, would regard a muscular dystrophy as a disease of nervous origin—a trophoneurosis. As I have already intimated, this is the opinion which I personally hold, and I believe that the future will see many changes in the chapters on the pathological anatomy and pathogenesis of these affections.

Before closing this chapter on the primary myopathies, I desire to say a word concerning the muscular atrophy of the *type Charcot-Marie*, not because I regard it as a muscular disease, for it belongs distinctly to the atrophies of nervous origin, but because certain authors have considered it as a transition form between essential myopathies and the myopathies due to nervous lesions. In its symptomatology and course this affection is certainly related to the myopathies which we have just been studying. The atrophy affects the lower extremities first and does not reach the upper parts until much later. It begins also during childhood, and often several children of the same family will be attacked. But alongside of these resemblances there are very wide differences. I have no intention to describe the symptomatology of this nervous affection here, and as regards the pathology it will suffice to say that the autopsy shows undeniable evidences of medullary lesions.

Thomsen's Disease.

This affection, which was very clearly described for the first time by Thomsen, a physician who was himself a victim, belongs to the class of primary diseases of the muscular system. Thomsen described it as a tonic spasm of the voluntary muscles consequent upon an hereditary psychic disposition, but we have no facts which would authorize us to refer the symptoms to any anatomical lesions other than those of a muscular nature.

Although this disease had been referred to in previous works, it

was not until 1876 that Thomsen, a physician of Kappeln in Sleswig, gave us a complete description of it based upon an exhaustive study of his own case. Since that time there have been many memoirs upon the disease, among others those of Erb, Ballet, and Marie. The two latter writers have defined the disease as consisting in muscular spasms occurring at the commencement of voluntary movements. This singular affection is referable to one essential etiological factor, viz., heredity. Dr. Thomsen had among his ascendants several persons affected in the same way as himself. According to the statistics, women would appear to be less liable to suffer from the disease than men. As indicated in the definitions given by Thomsen, Ballet, and Marie, the disease is a spasmodic one. Whenever the subject wishes to execute a movement, immediately the group of muscles whose action is necessary for the carrying out of his intention becomes stiff, and there is a momentary spasm which prevents all movement. Then gradually the rigidity disappears, the spasm relaxes, and the desired movement may be executed. The muscles of the lower extremities are as a rule more affected than those of other parts of the body, the greatest difficulty being experienced when the patient attempts to rise from a sitting posture or begins to walk. There is then a period of complete inability and the patient is forced to wait until the spasm relaxes before carrying out his design. After the spasm has relaxed and the movement is once begun there is nothing abnormal to be observed; but the whole trouble may be very easily caused to reappear, a mere change of direction, for example, being sometimes sufficient to excite another spasm. It is in military life that contractions of this kind have been most frequently observed. During drill the spasms are continually recurring, showing themselves each time a command is given to march or turn or make any other change in the order of movements. The condition is further aggravated by the mental disturbance caused by the knowledge that the orders of the commanding officer must be executed.

The muscles of the trunk, the neck, the jaws, the tongue, and the upper extremities may also in individual cases be implicated.

What do we discover here as regards the condition of the muscles? In the first place there is an hypertrophy, without, however, any increase in strength, rather on the contrary a diminution. During the occurrence of the spasm the muscles stand out prominently under the skin and give an impression of hardness to the hand. It is only the voluntary muscles that are affected. The reflexes are as a rule normal. Examination to determine the condition of the mechanical and electrical excitability of the muscular tissue has given interesting results. Erb has shown that the mechanical excitability is greatly

increased, the least touch being sufficient to excite a muscular contraction. The electrical excitability, both galvanic and faradic, is also increased. But the excitability, galvanic, faradic, and mechanical, of the nerves is rather diminished than augmented. To these alterations in muscular and nervous excitability Erb has given the name of myotonic reaction.

The *diagnosis* presents in general no difficulty if we bear in mind the clinical features which we have just sketched. In pseudo-hypertrophic paralysis, in which there is an apparent increase in volume of the muscles, there are never any spasmodic contractions. Hysteria is easily recognized by the other symptoms accompanying this condition, and besides the spasms do not yield with the same rapidity that they do in Thomsen's disease. The same applies to locomotor ataxia, in which the spasms are continuous.

As I have said before, the affection is a congenital one, the first manifestations of which appear usually in childhood or early youth. In many cases it seems to be associated with peculiar mental states, melancholia or hypochondria, and it was this that led Thomsen to look upon the affection as the consequence of an hereditary psychic disposition. The progress of the disease is very slow, but it may be accelerated by fatigue and overwork. Although an incurable disease it never compromises the life of the individual.

Up to the present time no lesions other than those of the muscles have been discovered, and in an account of an autopsy in a case of this disease which Déjerine and Sottas made to the Société de Biologie as late as June 21st, 1893, no mention is made of any changes in the central nervous system. Microscopical examination, according to Erb, Deléage, and Onanoff, shows changes in the muscular fibre, but few in the interstitial connective tissue. The muscular fibres are hypertrophied, the striations are less distinct, and the normal protoplasm is gradually replaced by a granular material. If there is any change whatever in the interstitial connective tissue it is at most a slight hyperplasia.

Treatment.—Thomsen's disease is resistant to all therapeutic measures, and no remedy has been found that is of the slightest benefit. Nevertheless it will be well to advise the patients to submit to systematic gymnastic exercises and methodical massage, in the hope that some benefit may accrue at least to the general health. Some authors, Erb in particular, have recommended the employment of electricity, either galvanic or faradic. But whatever measures we take we shall seldom be able to relieve the distress caused the patient by this spasmodic affection which deserves the name of infirmity rather than disease.

Secondary Trophic Troubles.

We shall not devote much time to a consideration of secondary trophic affections of the muscles. They are really an essential part of the diseases with which they are associated, and their description belongs rather to treatises dealing with these diseases. I shall, however, for the sake of completeness, review briefly their most striking features.

We may mention first among secondary trophic disturbances the atrophy consequent upon *inflammation of the muscles*. I have already remarked, in treating of myositis, how frequently atrophy follows upon inflammation, whether acute, subacute, or chronic, of muscular tissue. This group may be placed here as forming the connecting link between primary and secondary trophic disturbances. They are secondary in the sense that they are tributary to another disease, but they are related to the primary affections in that they are secondary to a disease wholly of the muscular tissue. Alongside of these atrophies it is proper to mention those which follow surgical affections of the muscles, such as wounds, ruptures, and contusions, the study of which has not occupied us in the present article.

Various local troubles may induce atrophy in the neighboring muscles. Thus diseases of the bones or articulations may interfere with the nutrition of the muscles in the neighborhood and finally lead to their atrophy. This might be called atrophy consecutive to *lesions in the vicinity*.

Then we have atrophies produced by what I would call *functional inertia*. In order to maintain itself in a normal state of nutrition the muscle has need of movement; and we know that exercise or massage, which is a form of passive exercise, exerts a very happy influence upon the growth and vitality of the muscular tissue. Therefore whenever for one reason or another a segment of a limb is immobilized we find a diminution in volume of its muscular tissues. This is because the circulation is less active and therefore nutritive material is brought to the part in greatly lessened amount.

We have next to mention the trophic affections secondary to *dyscrasiæ*. In this group of dyscrasiæ I include all acute or chronic general diseases which induce alterations of a nutritive character in the muscular tissue. In studying the various forms of myositis we saw that the infectious febrile diseases often induced inflammation of the muscles. But myositis is not the only affection so caused, and we even more frequently see atrophy of the muscles. Indeed there is nothing more common than to observe a very considerable atrophy

following an attack of typhoid fever, and it is also often seen after small-pox, measles, diphtheria, and other acute diseases. It has been observed in malaria, and is of common occurrence in tuberculosis and cancer. In a word, whenever for one reason or another assimilation and nutrition are defective there is more or less marked inanition, and the muscular tissue, like all the others, suffers and undergoes atrophy to a greater or less extent.

Various *poisons* exert a baneful influence on the muscles. I refer here only to chemical poisons and do not include in this category the poisonous products of bacteria—the toxins. I have in view especially two important substances, lead and alcohol. Mercury does not in general induce atrophy of muscular tissue.

The atrophy of lead poisoning affects chiefly the paralyzed muscles, which are ordinarily the extensors of the hands and fingers, but atrophy has been observed alone not preceded by paralysis. Cases have been seen of lead atrophy of the hands which presented all the appearances of muscular atrophy of the Aran-Duchenne type, which will be referred to below.

In chronic alcoholism there are often muscular atrophies affecting chiefly the lower extremities and sometimes producing deformities of the feet. These trophic troubles consecutve to alcoholic poisoning are, it must be said, under the direct influence of lesions of the peripheral nerves and ought perhaps to be described in the group of atrophies following nervous diseases, but the first etiological factor being an intoxication it seems more suitable to group these among the toxic atrophies.

We will now discuss very briefly the muscular atrophies consecutive to *diseases of the nervous system*, but will not enter into any details of symptomatology or pathological anatomy, as that would lead us into a description of all the nervous diseases in which any affection of the muscles occurs. For this the reader must be referred to the later volumes of this series, in which these diseases will be treated of at length. We must content ourselves here with a simple enumeration of the various maladies of the nervous system in the course of which muscular atrophies are observed.

In the first rank of these affections come the diseases of the spinal cord. Atrophy of the muscular tissue is not rare in locomotor ataxia; it belongs as a rule to an advanced period of the disease, and not infrequently leads to a characteristic deformity of the foot known as tabetic club-foot. In the upper extremities we find atrophies of the Aran-Duchenne type, that is, symmetrical atrophies beginning in the abductor brevis of the thumb and advancing to the hands and

upper extremities. In Friedreich's disease there is sometimes atrophy affecting certain muscles of the trunk or limbs.

But the type of muscular atrophy produced by medullary lesions is certainly that represented by the disease known since the description of Aran and Duchenne as *progressive muscular atrophy*. As we have just seen, this affection always begins in the hands and invades successively and symmetrically the segments of the upper extremity, passing thence to the muscles of the trunk. We have seen in the section on primary trophic disturbances of the muscles that Duchenne at first confounded this myelopathic atrophy with another form not accompanied by appreciable nervous lesions which we have called progressive myopathic atrophy. It is in progressive muscular atrophy that one observes the characteristic deformities of the hand called variously claw-hand, monkey-hand, *main en griffe, main de squelette.*

The other diseases of the spinal cord, scleroses and inflammations, are frequently accompanied by muscular atrophies.

There are certain forms of muscular atrophy consecutive to diseases of the brain. It is not uncommon, indeed, to observe atrophy of the paralyzed and contractured muscles after hemorrhage or softening of the brain. Descending scleroses affecting directly the muscles may follow these lesions.

Finally we have the entire category of peripheral neuritides which may induce a diminution of volume of the affected muscles. The type of these forms of peripheral neuritis is alcoholic neuritis. I have referred to this in speaking of muscular atrophies of toxic origin.

After this general sketch of the etiology of secondary trophic affections of the muscles, we may represent the subject graphically in the following table:

- Secondary trophic affections of the muscles may be caused by
  - 1. Inflammations.
  - 2. Lesions of neighboring parts.
  - 3. Functional inertia.
  - 4. Dyscrasiæ
    - Acute diseases: Typhoid fever, small-pox, erysipelas, etc.
    - Chronic diseases: Tuberculosis. Cancer.
  - 5. Poisoning: Lead. Alcohol.
  - 6. Nervous Lesions
    - Central
      - Medullary: Locomotor ataxia, progressive muscular atrophy, sclerosis, various forms of myelitis.
      - Cerebral: Hemorrhage. Softening.
    - Peripheral.....Neuritis.

Treatment.—There are two points to be considered in the therapeutic management of the case when the presence of these muscular troubles has been determined. In the first place we must address our efforts to the relief of the primary causal affection, and secondly endeavor to bring about an improvement in the muscular condition. We must therefore determine the cause of the trouble, and if possible remove it. For example, when the muscular affection is consecutive to a lesion of the brain or cord we may suspect the presence of syphilis, and may administer, occasionally with profit, large doses of iodide of potassium to which may be added some mercurial preparation. For the relief of the atrophy we must have recourse to massage and electricity under its different forms. It is well to say that the results of this treatment will often be far from brilliant, especially when the troubles are consecutive to lesions of the nervous system.

We have now concluded the study of diseases of the muscles. I have been very cursory in the discussion of the secondary trophic disturbances, the consideration of which belongs to another part of medical pathology. Nevertheless I should have preferred to develop at somewhat greater length this as well as some other divisions of my subject, but it has for various reasons been impossible to carry out my desire.

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OBESITY.

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OBESITY.

History.

The possibility of the occurrence of the disease known as obesity or corpulence, and which is due to errors of nutrition such as the ingestion of unsuitable or excessive amounts of food, was undoubtedly present in the earliest period of development of the human race, at all times and places.

It is least likely to have occurred among those nations of antiquity which had to struggle for existence with their crude surroundings and whose food was procured by hunting and fishing. Besides, in the flesh of game and fish they possessed a diet which even when consumed in large quantities had the least tendency to favor the deposition of fat.

The conditions changed with the increase of cattle raising and the invention of agriculture, especially with the discovery of the grape and the production of wine in the south, and the preparation of mead and beer from barley and hops in the north. These furnished opportunities for the consumption of food and drink rich in fat-forming substances and alcohol, which by their pleasant taste and intoxicating effect induced the ingestion of amounts beyond the needs of the body. Hence we find in early times personifications of indulgence and its consequences in mythological figures, in the well-nourished Bacchus and the pot-bellied Silenus in the south and in the legendary fat king of Flanders in the north.

With the progress of civilization and general prosperity among the nations, bringing in their train greater ease of living and love of enjoyment, especially in southern countries bordering on the Mediterranean, the occurrence of obesity with all its evil consequences became more and more common. For this reason the state took charge of the nutrition and education of its adolescents among those nations whose existence and government, whose cultural development rested upon the vigor and fighting power of their citizens, and upon the highly trained sense of the beauty of form, like the old Greeks and Romans. The laws of Lycurgus were thorough hygienic measures

against obesity, laziness, muscular weakness, and stupidity among the Spartan youth and the people in general.

The closely observing physicians of antiquity were as fully alive to the evil results of obesity as were the statesmen. Hippocrates was acquainted with the slight power of resistance of the corpulent against febrile diseases, with the coincidence of obesity and sterility in women, with the shortness of life and the occurrence of sudden death in fat persons, and gave strict directions for the prevention of the disease. A hard couch, severe physical labor in the early morning before breakfast, vegetable diet, especially the ingestion of greens, hardening of the body in the open, the prohibition of warm baths and of the use of wine unless largely diluted with water, were among his prescriptions.

The later physicians of antiquity, too, Celsus and Galen, gave strict directions against obesity, which the latter author ascribed to the preponderance of phlegm, one of the cardinal humors of his system. He was also aware of the dangers to life, the occurrence of sudden death, and the putrid (asthenic) character of the pyrexia in febrile diseases in such patients. The directions of the physicians of this period had to do chiefly with the somatic relations and external influences—exercise in the hot sun, the use of baths, especially sea baths (Celsus), vigorous frictions of the body (Cœlius Aurelianus). The influence of nutrition was but little understood in antiquity and the directions in this respect possess merely the character of general restrictive courses.

In the Middle Ages up to recent times no particular progress was made in the knowledge and treatment of obesity. Even the publications from the seventeenth and eighteenth centuries, containing chiefly mere descriptions of isolated cases of excessive corpulence and its evils, supply nothing new regarding the pathogenesis of the disease nor do they augment the therapeutic resources against it. Mention need be made only of the attempt of surgeons to proceed against obesity by operation and to excise the monstrous and cumbersome masses of fat. Thus a German prince, desiring to become thin, had a physician from upper Italy remove his fat, but unfortunately he died from the operation. It is reported of Rhotonet, a surgeon of Paris, that he in 1718 excised nine pounds of fat from the abdomen of a well-known person and thus relieved her. While during the seventeenth century but few physicians like Panaroli, Sebitz, and Wolf published papers on obestiy, the number of dissertations and treatises which have since appeared in France, England, and Sweden has increased considerably; but they contain nothing new in the pathology of the disease

and change or add but little with reference to the well-known therapeutic resources.

It was not until the nineteenth century, as a result of the labors of Justus v. Liebig with regard to the formation of fat in the animal body, that we not only gained a wider knowledge of the origin of superfluous masses of fat and the deposition of fat, but that we could also devise ways and means directed against the cause and nature of the disease for the prevention or restriction of its grave sequels. The dietetic Banting treatment by Dr. Harvey is based precisely upon the principles governing nutrition, especially in lessening the deposit of fat and in the consumption of the fat in the body. Banting's letter about the result of the treatment and his falling away was the cause of Harvey's method of reducing obesity becoming known by the name of the patient, and of its extensive use both in England and on the Continent. Under the circumstances it was inevitable that the faults inherent in the method should manifest themselves more or less markedly in various cases and stages of obesity and should thus limit its further application by unfavorable results.

Our knowledge of the formation of fat and of nutrition first pointed out by Liebig was enlarged in later years by the addition of some facts not fully understood by this investigator, namely, the origin of animal fat from carbohydrates and a more complete comprehension of nutrition, which resulted from the important labors of M. v. Pettenkofer, C. v. Voit, J. Munk, Shubotin, Radziejewski, and others. Their labors disclose the manifold formation of fats from nutritive materials—albumin, fats, and carbohydrates—their consumption and deposition in excessive fat formation, the causes of this process, and the influence of fat and fat-forming materials upon the important presence of albumin in the body. In the field of histology the investigations regarding the importance and development of adipose tissue and the formation of fat have not yet come to a harmonious conclusion, and the theories of Toldt, Flemming, Virchow, and Unna are in irreconcilable contradiction. In the field of pathology the labors of Leyden regarding sclerosis of the coronary arteries must be specially emphasized, since they threw light on the grave heart trouble which so frequently complicates obesity. The same author also more clearly defined the meaning of the term fatty heart.

By the widening of our chemico-physiological knowledge of nutrition the treatment has been placed on a firmer basis and it has been made possible to devise comprehensive scientific methods. The Banting method suggested by Harvey was introduced into Germany by Vogel and adapted to the conditions there prevailing. Subsequently Ebstein devised a new method which differed from the latter, owing

to a misunderstanding of Voit's labors, in not advocating a special restriction of the consumption of fat as opposed to the carbohydrates and which placed the supply of albumin far too low. Oertel's mode of treatment had reference not only to the restriction of fat and the maintenance of the amount of albumin, but also to the favorable influence of the diminution of water in the body upon the reduction of fat and upon the sequels of the disease, while it aimed to prevent and lessen the weakening of the heart muscle and the circulatory disturbances dependent upon it. The same author has moreover established sanatoria in various hilly and mountainous regions of Germany, Austria, and Switzerland, where methodical and strictly supervised exercises in the shape of walks and mountain climbing can be performed so as to furnish the necessary mechanical labor and insure the combustion of fat which is its object. Quite recently the question has arisen whether a reduction of fat can be effected by a dietetic-mechanical treatment without the loss of albumin; this has been answered in the affirmative by v. Noorden, who has pointed out the ways in which losses of albumin may arise during the treatment.

Inasmuch as obesity and corpulence are not amenable to medicinal treatment, we find in the history of the disease no remarks bearing upon the subject. The effect of drink-cures by waters containing sodium sulphate (Marienbad, Tarasp, etc.) can thus far be said to rest merely upon the fact that they remove a portion of the albuminous and fat-forming substances consumed in the food, by which the nutrition is lessened. These springs, therefore, in cases in which they are indicated, can at most but supplement the dietetic-mechanical treatment.

Finally mention should be made of hydrotherapy, which endeavors to utilize the heat-regulating effect of cold baths against corpulence. The combustion of fat necessary to increase the bodily temperature, however, is so slight that hydrotherapy likewise is to be enumerated merely as an adjunct to the above-named modes of treatment.

Etiology.

The main constituents of the human body by whose deposition and transformation it is built up and maintained are, aside from inorganic salts and ingredients of the ash, albumin, fat, and water.

Of these three constituents albumin and water are present in the normal organism in a proportionate quantity which does not vary materially; the former amounts to 15 or 16 per cent. of the weight of the body, while the latter varies only between 58.5 and 65.7 per cent.

(Moleschott), except after an abundant ingestion of fluid, when the blood and the tissues temporarily contain more water.

The fat alone, even in the healthy body, exists in such a variable quantity that the limits are wide apart and can only approximately be determined as ranging between 9 and 23 per cent. of the body weight. The total amount in general is also apt to be greater in women than in men, the proportion being as 16 to 13.5 per cent. Besides, within the limits of health the quantity of fat which is to be considered as normal varies according to the age, constitution, occupation, family tendency, season, climate, and racial peculiarities.

The use of the fat in the body is due to its chemical and physical properties.

The fat, being inclosed in vesicles whose membrane, saturated with water, can bear strong pressure without allowing the oily contents to escape, forms in its physical quality a thick elastic layer on the surface of the body, fills up interspaces and depressions between organs, bones, ligaments and muscles, protects against blows and other mechanical injuries, and contributes to the physical beauty of the body. Being a bad conductor of heat it furthermore protects the tissues which it covers and envelops against refrigeration; this applies not only to the panniculus adiposus with reference to the surface of the body, but also to the fatty omentum with regard to the intestine which is so sensitive to changes of temperature. Lean persons and old people whose fat is partly consumed are therefore more sensitive to a fall of the external temperature than others who are shielded by an ample layer of adipose tissue.

In a chemico-physiological relation fat serves in the animal economy by its combustion for the production of force and heat and thus prevents waste of albumin in metabolism. These qualities impart to fat a considerable influence on general nutrition and the physiological functions, and we shall have to study them carefully with reference to excessive formation and accumulation of fat, as well as to the attempt to reduce the amount of this substance in the body.

The fat in the body is formed by cellular elements from the lipogenous material, fat and carbohydrates, which reaches the blood by way of nutrition and is supplied to them. Decomposition products of albumin can likewise be changed into fat. The fat cell *per se* is capable of considerable metabolism. The fat formed in the fat cells may sooner or later be again decomposed, whereby diffusible substances develop which pass through the cells and are absorbed by the blood. When the state of nutrition is good this process probably takes place constantly, so that the same fat does not remain for years in the cells, but is ever decomposed and re-formed.

The fat which has become superfluous is inclosed in the body at the points of its formation in the fat cells; these, being fastened together by connective tissue, represent the adipose tissue. Regarding the origin of the adipose tissue two different theories have been advanced by histologists.

According to Toldt adipose tissue occurs in the body preformed as a normal tissue formation; it does not exist everywhere, but is lacking in the eyelids, auricles, scrotum, penis, clitoris, nymphæ, also in the muscular connective tissue of the intestine, etc. At these points, even under the most favorable conditions for fat formation, no appreciable deposition of fat occurs. At other points, however, both on the surface and in the interior, there are thick layers of this tissue in which according to circumstances large quantities of fat are accumulated. These points are, on the external parts of the body, the malar region of the face, the panniculus adiposus of the breast, the anterior abdominal wall, the pubic region, the sole of the foot, the ischial cushion, the lower and upper extremities. In the thoracic and abdominal cavities fatty tissue exists in the mediastinum, the epicardium, the surface of the heart, the mesentery, the greater omentum, in the appendices epiploicæ, the adipose capsule of the kidneys, and finally also in the intermuscular tissue of the voluntary muscles and the yellow bone marrow.

Adipose tissue, according to Toldt, must not be classed with the connective tissue either by its histological structure or by its functions. Its embryological development, too, does not proceed from the connective tissue but from definite germ layers, and in its further growth is connected with the preformed adipose tissue.

According to a widely differing assumption by Virchow and Flemming, there is no special difference between adipose and loose connective tissue, and the fat cells are said to be identical with the fixed connective-tissue cells. The connective-tissue cells and other cells may change into fat cells by the absorption of fat if they are favorably situated in relation to the blood current so as to take up the lipogenous material transuding more or less freely from the blood after the ingestion of food. The transudation from the vessel wall occurs in greater amount wherever there is a considerable retardation of the circulation by reason of a circumscribed dilatation of smaller vessels.

According to both theories, intimate relations exist between adipose tissue and the vascular apparatus, and a deposit of fat occurs only where there is a rich vascularization and retardation of the blood current, while tissues containing few vessels do not become filled with fat. The amount of the deposition of fat, however, rests withal upon conditions which vary with the individual and the time. Under the

assumption of a specific adipose tissue (Toldt), copious nutrition, slight tropho-plastic activity of the tissues, and deficiency of oxygen of the blood do not suffice for the accumulation of fat in the body; but the secretory energy of the adipose tissue, its quantity, and its power of proliferation enter largely into the consideration and therefore will differ in amount in various individuals and at different times. The amount of the accumulation of fat therefore may show extensive variations under otherwise equal conditions in a concrete case.

If we do not consider the adipose tissue as a special tissue formation, then the amount of the deposition of fat is based upon the vasomotor innervation and the irritability of the vessel wall dependent upon the more frequent or rarer occurrence of a local vascular dilatation in the loose connective tissue, and is influenced moreover by the number of cells in the adventitia and the power of proliferation of its cellular elements, which may show more or less individual variations. On the other hand, Toldt and his followers do not doubt that the connective-tissue cells produce fat under certain circumstances and accumulate it in their interior in larger or smaller drops. In advancing obesity, according to Toldt the preformed adipose tissue from definite germ layers will increase in extent and thickness, and at the same time more and more connective-tissue cells are changed into fat cells; while according to Flemming the deposition of fat takes place in the connective-tissue cells.

Recently Unna has advanced another theory of the formation of fat and the adipose tissue.

Unna assumes three sites for the formation of fat, the first of which is said to be in the skin, the second in the muscles, and the third in the intestine. In the skin the fat is produced mainly by the activity of the convoluted glands. The kidney fat he interprets as muscle fat, the fatty lymph current being filtered through the veins of the capsule of the kidney. The source of the intestinal fat is said to be situated in the mesentery where the fat is formed by the cooperation of certain blood corpuscles. Basing his argument on these results of his investigations, Unna has attempted to explain why one and the same method of forced nutrition and of fat-reduction cannot have the same effect on all the deposits of fat.

How far the facts will bear out Unna's views, which would be likely to advance materially our knowledge of the pathogenesis and the course of obesity, must be settled by future investigations.

Hence the pathogenesis of obesity is by no means as yet fully elucidated by the histological and physiological examinations bearing upon it. The frequent early development, the course, the rapid or

tedious involution of corpulence, especially by therapeutic measures, present absolutely unexplained phenomena observed not only in different cases but also at different times in a concrete case. Most incomplete, however, is our knowledge of the various factors which induce obesity, if we endeavor to trace its etiology and particularly to answer the question about the disposition to an extensive accumulation of fat or to obesity.

The decision whether the fat accumulated in the body has already exceeded the normal limit, whether it has led to corpulence, obesity (lipomatosis universalis, adipositas, obesitas, polysarcia, corpulentia morbosa), and occurs as a pathological phenomenon or a disease *sui generis*, will depend upon the following two criteria:

1. Whether the external proportional somatic relations and the symmetry of the limbs are disturbed by an unequal increase of volume in consequence of excessive deposition of fat; and

2. Whether a limitation of the functional activity of the various organs, especially of the circulatory and respiratory organs, is caused by an excessive accumulation of fat.

According to this limitation of the conception of increased fat formation and deposition, therefore, the abnormal development of fat such as occurs in fatty degeneration of the tissue elements and in processes leading to atrophy, is completely excluded and relegated to another chapter in pathology.

Causes of an Increased Formation and Accumulation of Fat in the Body.

The causes which lead to an abnormal formation and accumulation of fat in the body, to corpulence and obesity, are always to be traced ultimately to the fact that the fat-forming substances ingested with the food find their physiological utilization for the functions of the body only to a slight extent and therefore are deposited as fat in larger amounts in the above-mentioned reservoirs. The fat-forming substances in the food may either be within the limits necessary for the nutrition of the body, and hence relations and conditions may obtain in which even with normal nutrition there is economy and increased fat-formation; or else these substances are ingested in such quantities that it is altogether impossible for them to be used up in physiological processes for the development of force and heat, and hence, having become superfluous, they are changed into fat and stored in the reservoirs. In accordance with these facts we shall have to keep separate in the etiology a number of special causal factors.

1. *General Tendency and Hereditary Disposition.*

Experience teaches that not all men under equal conditions accumulate fat, but that many persons may be safely as immoderate in eating and as inactive as others in whom within a brief period an ample accumulation of fat in the body becomes perceptible and in whose families a pronounced tendency to an abnormal fat formation and deposition has been hereditary through many generations. Thus we find in the literature so large a number of cases recorded, and every practitioner has observed so many similar instances, that the hereditary disposition to corpulence is established as an undisputed fact. Statistics permit the assumption that among the corpulent patients coming under observation at least fifty per cent. have an hereditary tendency to this disturbance of nutrition.

The hereditary disposition usually manifests itself in early life by an abnormally great development of fat, either in all the children or only in a certain larger or smaller number; but on the other hand it may not appear until a more advanced age, especially under favorable nutritive conditions, either in all or in only a few members of the family, or in women after the first pregnancy. Furthermore, the hereditary tendency in general is said to be more frequent in women than in men. As in other hereditary taints, that leading to the hyperplasia of fat may skip one or more generations and pass from the father to the grandchild. But the statement that the heredity is more pronounced in the same sex, passing from the father to the son and from the mother to the daughter, has not been generally confirmed (Kisch). I myself have likewise thus far failed to find any confirmatory evidence.

To cite a few instances from the literature of obesity in early life: Barkhausen reports the case of a boy aged fifteen months weighing 35 pounds; Heyfelder, that of a girl aged three and a half years weighing 49¼ pounds; Kästner, that of a girl aged four years weighing 82 pounds; Benzenberg, that of a girl aged four years weighing 137 pounds; Weinberger, that of a boy aged five years weighing 189 pounds; Don, that of a Hindoo aged ten years weighing 266 pounds. In more recent times Wolf has described a new-born child weighing over 18 pounds. Kisch observed a girl of six weighing 110 pounds; one of eleven, 132 pounds; one of sixteen, 312 pounds. I myself have observed several families in which all the children, numbering two, three, and five respectively, showed an enormous development of fat; in one case a girl of seven weighing 124 pounds. It would not be difficult to swell these figures greatly with cases from the literature.

It is as yet impossible to give a satisfactory explanation of the causes upon which the hereditary tendency to an abnormal accumulation of fat in the body may be based. Many attempts have been made in this direction.

1. We might try to ascribe the cause to a congenital difference with reference to the quantity, functional and proliferative power of a preformed fatty tissue existing as an independent organ, or of the fat-bearing connective tissue with its vascular apparatus. The assumption is not without some supporting facts, since the question as to the histological character of the adipose tissue has not been finally decided, as there are different views concerning the formation and deposition of fat. *A priori*, therefore, the idea cannot be rejected that the hereditary tendency may possibly have an histological foundation and that the inherited quality of the preformed adipose tissue may become the predisposing cause of obesity.

2. We might also assume a congenital difference in the trophoplastic energy of the tissues of the body by which the amount of deposit of albumin may be determined. Persons whose albumin-bearing tissue, especially muscular and glandular tissue, exhibits a strong power of growth, in order to satisfy this cellular vital requirement need a larger amount of nutriment and therefore are less liable to become obese than others whose hereditary constitution lacks this energy of growth and nutrition.

3. An hereditary difference has been assumed with reference to the hypoplasia of the red blood corpuscles and slow regeneration of the blood and its hæmoglobin contents, but no proof of this difference has been furnished in disputed cases.

Cohnheim ascribes the disposition to accumulate fat under conditions which are normally without such effect to a faulty activity of the cells, that is, to a slighter energy of the oxidizing processes in the tissue cells, in which it is said the oxygen is combined with the fat supplied to them or occurring as a decomposition product. On the other hand, he leaves it an open question whether the hæmoglobin contents of the blood corpuscles are not too low, whereby the oxidizing processes are restricted.

Not only in men but also in animals has an hereditary disposition to fat hyperplasia been demonstrated. Roloff's investigations show that there are certain breeds of swine which are particularly suitable for fattening. This racial peculiarity is the result of a special mode of breeding which requires not alone an appropriate selection of the brood animals but also uniform and methodical feeding, rest, and fattening nutriment. When the procedure is continued through many generations we may observe the interesting fact that the production

of fat acquires quite an extraordinary energy, fat in excess accumulating even in the muscles and the cells of glandular organs, thereby lowering their functions.

Finally the fact deserves special attention that the adipose tissue reacts differently to reducing influences, in cases in which its hyperplasia is due to an hereditary disposition, or has been produced by abundant nutrition or forced feeding. In the latter class it is usually possible in a short time to make the excessive fat accumulated in the body undergo combustion by dietetic measures, etc.; while in the former class this reduction is far more difficult, so that the result is always but temporary in patients who are unable to carry out a suitable mode of life for a term of years and in whom the prognosis in general is more unfavorable. The varying behavior of fat hyperplasia in hereditary disposition and in acquired corpulence requires for its elucidation a more thorough study.

The hereditary factor is most closely related to the

2. *Antagonistic Nutritive Anomalies.*

Virchow first called attention to certain abnormal nutritive processes in adipose tissue, which presuppose a natural disposition to general hyperplasia of the fatty tissue or are prone to produce a partial form, even when the consumption of fat-forming substances in the food does not exceed the normal. These nutritive anomalies have not yet found a satisfactory explanation.

The cases to be first enumerated here are rare and should be kept apart from the ordinary cases of polysarcia because of their pathological peculiarities and defects. The obesity beginning at birth and increasing during childhood is termed by Chambers a kind of malformation in which the patients usually suffer from some other physical deformity, or from a lack of intelligence, or from some greater defects of cerebral development. An accumulation of fat which is often very great is found in acephalous monsters and was first observed and described by Lobstein; it occurs likewise in cretinous dwarfs, and Virchow has classed the obesity of the acephali with the latter. Treatment of course is hopeless.

Antagonistic nutritive relations exist moreover between obesity and the functional activity of the sexual organs and the nutritive relations dependent upon it, or between the absence of this activity and the loss or disease of the sexual organs. In men whose sexual activity ceases early or who have become impotent from any cause, or have undergone castration, we often observe a rapid increase of fat formation. In the same way fattening is effected more easily and

extensively in castrated animals—capons, oxen, and sheep. Not rarely, too, the adipose tissue of women is augmented considerably when menstruation ceases, sometimes also after the normal puerperium and prolonged lactation; in such cases, however, the conservation of nutritive material must be taken into consideration. In like manner women with insufficient exercise of the sexual function or young widows who live virtuous and care-free lives frequently become obese. According to a compilation by Tilt (Krieger), of 282 women whose menstruation had ceased for five years 121 had become obese, 71 had retained their normal figure, and 90 had become thinner. Moreover in women who are sterile in consequence of uterine or ovarian disease an increase of adipose tissue has been observed. There can also be no doubt that among religious celibates, some of whom live immured in monasteries (monks, nuns), the plentiful ingestion of fat-forming substances in their diet, especially during Lent, with their quiet life free from care and subject to few exertions, must contribute largely to the development of obesity.

A similar nutritive contrast would, according to Kisch, also explain the excessive corpulence of scrofulous children and the occurrence of lipomatosis after recovery from secondary syphilis.

Another disposition to increased formation of fat is furnished by

3. *The Influence of Age.*

It is known that the normal fat formation in man is influenced by the age, in connection with which the mode of nutrition, rest, and slight muscular activity are of decisive importance. The pathologically increased fat formation likewise depends materially upon the age and the conditions of life appropriate to it.

In infancy the fat production is maintained in especial manner by the milk diet as well as by the absence of great muscular activity, which favors the formation of fat; and nurslings who are artificially fed with farinaceous substances exhibit not rarely quite an extraordinary increase of adipose tissue. In adolescence, in which much nutritive material is used for building up the organism, and in advanced age which presents a continual consumption and retrograde metabolism in all the tissues, there is generally a lack of all the conditions which permit of an abnormal accumulation of fat in the body.

The periods that are most favorable for the development of corpulence and obesity are in men advanced middle age between the fortieth and fiftieth years, and in women the climacteric toward the end of the fourth decade of life, in which the ingestion of food and consump-

tion of material are most frequently in a relation favorable to the utilization and accumulation of fat. Thus statistics prove that the greatest development of fat in the male sex occurs in the period between forty and fifty years, and that the least production of fat occurs between fifteen and twenty years. In the female sex, however, the development of fat about the time of puberty, between fifteen and twenty years of age, is far greater than in the male sex. Furthermore the amount of fat development is nearly uniform in women during the decade between thirty and forty, and next to this during that between forty and fifty years, where the occurrence of puberty, the puerperium, and the climacteric favor the accumulation of fat (Kisch).

The age at which the congenital disposition to fat hyperplasia manifests itself has been already mentioned above. In general, opinions vary greatly. Many observers agree that in such cases an abnormal development and accumulation of fat occur even in earliest infancy. The obesity of such children, according to Meckel, presents the character of morbid and premature development. As a rule, however, the early fat hyperplasia undergoes a diminution. The fat formation returns to the normal and increases again in later years, either after puberty or at the time of greatest vigor, but most frequently in advanced age.

With the age of the individual, too, the location changes in which the excess of fat is deposited. This remarkable process seems to stand in a causal relation to growth. In embryos and the new-born the subcutaneous cellular tissue, the omentum, and the mesentery remain free from fat even when the deposit is great in other places. As long as the growth in height continues, but little fat is found in the internal organs, while during middle age large quantities are accumulated in the omentum, mesentery, pericardium, mediastinum, etc. In old age, on the other hand, the fat persists for a long time in the internal organs after that in the subcutaneous cellular tissue has largely disappeared.

4. *Sex, Physiological Constitution, and Temperament.*

Sex.—Even under physiological conditions the female body, in the roundness of its parts and the softness of its outlines, is richer in fat than the male figure, which is more muscular and has a more angular contour.

The cause of this phenomenon lies in the greater development of the adipose tissue, which in women is naturally more extensive than in men; while the blood, being poorer in hæmoglobin, is less favor-

able to the oxidation of the fat-forming substances in the food, so that their transformation into fat and deposition in the adipose tissue can occur to a greater extent. As these differences between the two sexes can be observed even in infantile life, they must of course become more pronounced in later years during which nutrition and habits favor the formation of fat far more in women than in men, especially in those cases in which the development and deposition of fat appear as a morbid phenomenon.

We shall have more to say hereafter about the differences in fat formation, and the forms of obesity dependent upon them; these in women are not so much caused by excesses in eating and drinking, for which reason women are less liable to be lampooned and made sport of than men.

Physiological Constitution.—The conditions known as constitution and temperament have, as the facts prove, no inconsiderable influence upon the formation of fat. The constitutional tendency and the temperament may be of hereditary origin and constitute influential factors in the hereditary disposition. In the constitution it is mainly the relaxed or torpid type which is characterized even under normal conditions by weakness of the organic regenerative power and the slight capability of transforming the circulating albumin into organ albumin. One of the chief causes which produce these conditions lies in the hypoplastic anæmia, in the slight hæmoglobin contents of the blood, in the decreased absorption of oxygen, and in the lessening of the oxidation processes in the body.

Since under such conditions there is not only an ample formation of fat from the circulating albumin, but also a slight combustion of the fat-forming substances, especially carbohydrates which these individuals consume in large amounts, the body contains an excess of material for the formation and deposition of fat.

Temperament.—The slight energy of the psychic functions, of the impulses and passions, and the trifling changes in the emotions which constitute the nature of the phlegmatic temperament, furnish an additional factor in the individual disposition to corpulence. Opposed to this stands the choleric temperament with its ready excitability, violent impulses, abrupt changes of the emotions and passions, and bustling activity, which are unfavorable to the accumulation of fat. Both temperaments probably are ultimately based upon the physiological constitution—on the one hand, relaxed, torpid, and characterized by hypoplastic anæmia; on the other hand, erethistic, excitable, and characterized by quick irritability of the nervous system and by increased energy of the oxidation processes due to a blood rich in hæmoglobin.

The phlegmatic temperament includes a number of factors which favor the formation and deposition of fat. The desire for rest and comfortable enjoyment induces the phlegmatic person not only to avoid every extensive fatiguing muscular activity, but it also reduces the uncontrollable muscular movements in daily life which in the choleric become innumerable.

The choleric moves ten times before the phlegmatic decides upon a single movement, and while the choleric forgets to eat for his mental and physical exertions, bustling activity, and psychical excitement, the phlegmatic seldom allows himself to be disturbed at his long and extensive dinner or in his sound sleep afterward. In ordinary life and in the arts too, the phlegmatic and choleric are typical figures for obesity and leanness, for quiet contemplation and mental excitability, for indisposition to physical exertion and restless activity, carousing, and excesses.

There is no doubt that the psychical and physical peculiarities which we summarize in the temperament have an accelerating or retarding influence upon the consumption of food, the nutrition, the metabolism, and the production of fat; in the one case furnishing the cause for an accumulation of fat, in the other for an extensive combustion.

As regards, however, the personification in the opposite sense of the corpulent as a phlegmatic, indolent, dilatory individual opposed to physical and mental effort, as a Silenus and Falstaff, we do not find it always fitting, and history teaches that men of superior intelligence, energy, activity, and vigor may be obese.

5. *Faults of Nutrition.*

The following section of the etiology is the most important in the disease now under consideration. Not only do the preceding etiological factors materially depend upon the influence of a faulty nutrition, but the latter by itself is capable of causing an overproduction of fat, corpulence, and obesity, in persons in whom the former etiological factors are absent. In order to study the injurious effect of defects of nutrition we must distinguish:

a. Those due to the ingestion of excessive and improper food; and

b. Those resulting from an insufficient assimilation.

Both faults of nutrition may be and generally are present at the same time; but the latter process may suffice to produce an abnormal accumulation of fat, especially when the preceding etiological factors act in combination with it.

a. *Faulty Nutrition.*—The animal body consumes for the mainte-

nance of the absolutely necessary vital functions, when at rest, a certain quantity of albumin, fat, carbohydrates, and water; and this amount is increased according to the labor performed by the body, especially muscular labor. If the ingestion is restricted to the amount of albumin, fat-forming substances, and water required under these circumstances the body maintains its equilibrium. If the ingestion of these substances exceeds the requirements, then with the rapid decomposition of albumin the non-nitrogenous constituents separated from it and the excessively ingested fat-forming substances are changed into fat and deposited in the tissues. The excess of water consumed is under normal conditions rapidly excreted with the utilized materials in the urine, sweat, and insensible perspiration. The temporary requirement of our body in the way of nutritive material therefore will vary according to its resting or active condition, regard being had also to the age. As this requirement is of decisive importance in the treatment of obesity a more detailed consideration of it becomes absolutely necessary.

In the following tables the temporary requirement of nutritive material is noted according to age, rest, and muscular activity:

1. Requirement of Nutritive Material in Childhood, from Four Months to Fifteen Years, the Muscular Activity or Rest Being Appropriate to the Age.

	Albumin.	Fat.	Carbo-hydrates.	Author.
1. Child of 4 to 5 months (condensed milk)	21	18	98	Forster.
2. Child of 18 months (mixed food)	36	27	150	"
3. Children of 6 to 10 years	69	21	210	Hildesheim.
4. Children of 6 to 15 years (Munich Orphan Asylum)	79	35	251	Voit.
5. Children of 6 to 15 years (Frankfort Orphan Asylum)	62	25	300	"
6. Up to 15 years	75	20	250	Simler.

2. Nutritive Requirements for Persons Doing Little Work or Resting, either Voluntarily or from Force of Circumstances.

	Albumin.	Fat.	Carbo-hydrates.	Author.
1. Nutritive requirement, minimum.	66	24	330	Playfair.
2. Nutritive requirement, maximum.	119	51	530	"
3. Laborer at rest	137	72	352	Pettenkofer & Voit.
4. Poor woman	76	23	334	Forster.
5. Beneficed woman	80	49	226	"
6. Prisoner without labor	87	22	305	Schuster.
7. Poor laborer of small capacity	86	13	610	Hildesheim.
8. Poor London seamstress	54	29	292	Playfair.
9. Trappist monk	68	11	469	Voit.

3. Nutritive Requirements for Persons Performing Prolonged Muscular Labor.

	Albumin.	Fat.	Carbo-hydrates.	Author.
1. Strong laborer	137	173	352	Pettenkofer & Voit.
2. Porter	133	95	422	Forster.
3. Joiner	131	68	494	"
4. Strong old man	116	68	345	"
5. Italian brick-worker	167	117	675	H. Ranke.
6. Woodman in Reichenhall	112	309	691	Liebig.
7. Woodman in Oberaudorf	135	208	876	"
8. Field laborer in Laufzorn	134	108	788	H. Ranke.
9. Miners at Silberau mines	133	113	634	E. Steinheil.

The ingestion of food beyond these quantities will necessarily be followed by an accumulation of fat in the body. The extent of the over-production in that event is dependent upon the amount of the ingested food, upon the existence of an individual, especially an hereditary, disposition to fat hyperplasia, and furthermore upon the laws governing nutrition. A nutrition which is effected with an overproduction of fat coincides absolutely with the fattening of animals, and the rational principles underlying the latter apply exactly to the former. Therefore, wherever increased fat-formation comes under consideration, as in forced feeding, the quality of the nutrient material will always be of paramount importance, and in the etiology of corpulence such foods as are easily changed into fat and substances which serve to economize fat will deserve special attention.

a. Foods Favoring the Formation of Fat.—It was Liebig who, basing his belief on the experience that domestic animals are best fattened by being supplied with food rich in carbohydrates, taught that the chief and preferable fat-formers are the carbohydrates, by the side of which the fat in the food plays only an inferior rôle, especially since the animal fats are altogether different from those contained in the food.

Later, when Virchow demonstrated a fatty metamorphosis of the albuminous protoplasm in the pus, epithelial, and glandular cells, these observations of course could find no application to the physiological processes of nutrition so as to lead to the assumption of a development of fat from albumin. It was Pettenkofer and Voit who showed, by experiments on dogs, that it was probable that from the decomposing albumin fat is formed, or at least a substance rich in carbon from which fat develops by synthesis. On feeding a large dog experimentally with 400 gm. albumin daily, all the nitrogen of the albumin had reappeared in the urine, but not all the carbon in the expired air and the urine; hence a decomposition product, rich in

carbon, of the albumin had remained in the body, and this they believed to be fat. Moreover, it was observed by Subottin, Voit, and Kemmerich that a suckling bitch exclusively and plentifully fed with meat furnished the greatest amount of milk rich in fat. By these experiments the proof of the formation of fat from albumin was thought to be established.

On the other hand, however, the question was raised whether the excess of the fat in the food is really deposited as body fat in the organism, and whether it is not rather the fat in the food which is decomposed and only that fat is stored up which is formed from the decomposed albumin. It was necessary, therefore, to furnish the proof that fat likewise, if fed in excess, may be directly deposited in the animal body, and this proof could be supplied only by feeding with a fat which does not occur in the animal body and whose subsequent accumulation alongside of the animal fat was to be demonstrated. Experiments in this direction were first undertaken at Kühne's instigation by Radziejewski, who fed with rape oil, but without obtaining decisive results. Later on Lebedeff succeeded in causing the deposition in the dog both of the tallowy hard sheep's fat and of the liquid linseed oil supplied in the food. The question was finally decided only by J. Munk, who showed that after feeding for two weeks with rape oil along with a little albumin there was deposited in the body of a dog nearly 1.5 kgm. of an oily fat in which also the characteristic constituent of rape oil, erucic acid, could be recognized. Thereby the transition of the food fat into body fat was settled beyond a doubt. Ebstein's view, that fat in the food does not give rise to fat-formation, is one directly opposed to all physiological investigations, and, as Zuntz has shown, has arisen only from a misunderstanding of one of Voit's statements, whose interpretation in Ebstein's sense has been particularly cautioned against by Voit himself, for which reason it may be passed over as unscientific.

According to Pettenkofer and Voit, the carbohydrates contribute in the main indirectly to the formation of fat. Being easily decomposed, they may even in the largest quantities be completely oxidized into carbonic acid and water, and thereby save both the fat of the food and that formed from the altered albumin from decomposition. Further experimental investigations, however, by Weiske and Wild, Soxhlet, Meissl and Strohmer, J. Munk, M. Rubner, and others have definitely proved also that fat is formed in the animal body directly from carbohydrates.

The fat-formation in the human body is therefore amply provided for by the food in its varied composition. Body fat may be developed from the fat ingested in the food, even from the preformed fatty

acids or those derived from the fats and soaps, as well as from the carbohydrates and the albumin. Voit has calculated that a formation of fat occurs in a man at rest or doing little work whenever he ingests along with a sufficient quantity of albumin (118 gm. daily) more than 259 gm. of fat, equivalent to 624 gm. carbohydrates, or more than 100 gm. fat and 385 gm. carbohydrates. When this quantity is permanently exceeded, some fat is daily deposited so that in the course of time the accumulation of fat may become quite large.

b. Insufficient Utilization of Material.—The body fat and the fat-forming substances ingested in the food, together with the carbonaceous decomposition products of albumin, are more or less completely consumed in the animal economy for the production of force and heat, in which case they are split up into carbonic acid and water. The amount of the fat combustion is nearly proportionate to the labor performed. All the physiological functions, too, are effected with a decomposition of fat, and the production of heat is directly dependent upon it. The greatest combustion of fat and fat-forming substances is required for muscular labor and may rise, according to the extent of the work, to more than double the normal fat transformation occurring at rest. It is true, Pflüger and his pupils, Krummacher and Argutinsky, have recently felt compelled, on the strength of their experiments, to assert that the muscle works with albumin; but von Noorden and Munk have pointed out the errors in their observations, since the increase of albuminous transformation in Pflüger's experiments was dependent upon the deficit in calories and thus was only loosely connected with the muscular labor as such (Munk). Pflüger's view, that the albumin is the source of the force, is vitiated, according to von Noorden, even by the calculation which shows that men utilizing day by day more than half of the entire calorie transformation in muscular labor, ingest year after year at most 14 to 18 per cent. of the entire calorie value as albumin in the food. In view of this fact, the assertion that albumin is the source of muscular force would contravene the law of the conservation of energy.

As in the requirements of active labor, so where greater heat formation is called for, more fat must be used up. This is in harmony with the experiments which show that a low temperature of the surrounding air raises the combustion of fat, while it has no influence upon the decomposition of albumin. For this reason a diet suitable for the requirements of winter will lead to the deposition of fat in the summer.

We know from the experiments by Beclard, Moleschott, Pflüger, Voit, and others that the most variable stimuli acting upon the sen-

sory nerves are followed by an increased metabolism which is associated with augmented decomposition of fat, while the intensity of the metabolism is materially lessened when such influences are absent. The cessation of sexual activity in animals after castration hastens their fattening, according to the experience of cattle breeders (see above). In accordance with these facts, too, the decomposition of fat is at the minimum during sleep. In Liebermeister's experiments the excretion of carbonic acid per hour sank during sleep from 32.8–33.4 gm. to 24.6 gm. From this fact Lobisch calculates that a person who changes his mode of life, the supply of food remaining the same, by sleeping eight hours instead of seven, accumulates in the course of a year 1 kgm. 43.9 gm. (about $2\frac{1}{3}$ pounds) more fat in the body.

An insufficient combustion of fat with the consequent proportionate accumulation of fat in the body as compared with the fat-forming substances ingested with the food seems to depend also upon the condition of the blood in which its contained hæmoglobin is diminished, whether by a lessened number of blood corpuscles in general or by a smaller amount of hæmoglobin in their normal number, in anæmia and chlorosis. The restriction of the oxidation processes in consequence of the slighter absorption and distribution of oxygen would partly explain the experience of physicians that a rapid development of fat occurs as an unwelcome symptom of chronic ill-health, in the early stages of grave diseases, in pulmonary phthisis, scrofulosis, secondary syphilis, pernicious anæmia, etc., in which cases of course the fat soon disappears again; and in like manner that after a severe sickness and great losses of blood not rarely a high degree of corpulence develops. Since in cases of convalescence from typhoid fever, scarlatina, etc., the attempt is frequently made to counterbalance the losses in a hasty manner by an ample supply of food, while there is no particular muscular activity, such nutritive processes resemble the fattening of animals which have first been partly deprived of their albumin by fasting and then are rapidly made fat by the forced feeding.

Under the conditions named—insufficient bodily activity and excessive rest, too much sleep, a life free from care and excitement, pronounced phlegmatic temperament, anæmia and loss of albumin—the possibility exists that even under a mixed diet containing enough albumin and fat-forming substances an increase of the body fat will gradually take place. The fat production is quite inordinately enhanced, however, when, besides such substances, fat, starch flour, sugar, etc., are ingested in large quantities, as is done by gourmands, great eaters, and by women (cakes, candy, etc.). This is true particularly of excessive beer drinking, by which usually so large a quan-

tity of fat-forming substances is taken into the body that it is no longer possible to burn them up completely even during laborious muscular activity, as in the case of brewers, bakers, butchers, etc.

As regards the alcohol in such cases or in general, the investigations are still insufficient to show how it acts on the combustion of fat. According to the investigations of Forster, J. Munk, and others, if used in moderate, non-intoxicating quantities it lessens the excretion of urea and also (Zuntz and Geppert) that of carbonic acid; hence it acts similarly to carbohydrates and fat, as, being burned up in the body, it may save an equivalent amount of albumin and fat. But it differs altogether from the latter nutritive materials, when consumed in larger intoxicating amounts, in that it increases the decomposition of albumin in the body and must lead to a correspondingly augmented fat-formation from the latter. In this respect the alcohol ingested with large quantities of beer and that contained in brandy are absolutely identical, and the fatty degeneration of the various cellular elements usually occurring in drinkers bears out this statement; only the large amount of carbohydrates in the form of dextrin, maltose, etc., ingested with an over-abundant consumption of beer leads to an even greater deposition of fat, as observed chiefly in countries where beer is the favorite beverage. To these facts and their sequels I endeavored to call special attention fifteen years ago in my "Manual of the General Treatment of the Circulatory Disturbances" (first edition, 1884).

In this connection mention should be made also of the ingestion of fluids in general and their influence upon the decomposition of fat. I first gained the experience in 1875 in my own person, and since then have observed in numerous patients under conditions which admit of no cavil, that the involution of fat-formation, reduction of obesity, takes place in the shortest time when little fluid is taken, while the weight decreases more slowly or rises again when the amount of liquids is increased. I have attributed the cause largely to unfavorable circulatory and oxidation processes, especially when in consequence of an excessive accumulation of fat there have resulted circulatory disturbances—congestions—which are always unfavorably influenced by the ingestion of fluids. Besides we know from the investigations of Voit, cited by Lorenz in his observations, that the decomposition of albumin increases under a free ingestion of water, when the particles of the albuminous solution are carried past the cells by a more active flow of the tissue juices. When the water supply is limited the decomposition of albumin would be diminished and, as the power of the cells is not yet exhausted by the slight decomposition of albumin, the fat distributed in the lymph current

might undergo combustion. The loss would then later on be made good by the fat passing from the adipose tissue into the lymph current. In this process it is self-evident that it is never organ albumin but only circulating albumin which undergoes combustion, in the same way as body fat is never oxidized without having first been distributed in the lymph current. On the other hand, according to this explanation, even when the ingestion of water is increased a lesser combustion of fat would occur, since it has been demonstrated by Voit, J. Munk, and others that under those circumstances more albumin is decomposed by the cells, and so new fat might form from the decomposition products of the albumin which are rich in carbohydrates, or else the fat-forming substances contained in the food would be changed in larger quantities into fat by their oxidation.

Quite interesting are the results of the experience of the English trainers Symes, Maclarn, Worthington, Baelz, etc., with reference to the reduction of corpulence. Among the directions for training, both in England and in America, is the recommendation to use drinks in great moderation or even to abstain from them altogether (one-half pint [one-quarter litre] of tea with every meal). The food is not of so much consequence, only very fat dishes are to be avoided, but whatever is eaten should be so prepared as to contain little water, and since meat which is boiled down or fried is said to retain little water it would be appropriate for the reduction of fat. At the same time the abstraction of water from the body is aimed at in every way, by increased perspiration and by laxatives, especially sulphate of magnesia (in 40-gm. doses). According to the further experience of the trainers an increased ingestion of fluids—several glasses of water or beer—is said to raise the body weight at once by several pounds. The same statement, that during the reduction of obesity an increased consumption of liquids (water) may immediately raise the weight again, has been for years repeated to me by observing patients.

Confirmatory observations as to the influence of diminished ingestion of fluids upon the reduction of fat are on record in large number by Lorenz, Rapp, Hausmann, Glax, Mazepper, A. Schmidt, and others.

As to the results of fattening animals by the aid of a plentiful ingestion of water Dancel may be cited; otherwise no experiments in this direction have been published.

Finally the development of fat is said to be favorably influenced, according to the observations on syphilitic patients, by treatment with mercurials (Kisch) and, in accordance with general experience, by the use of arsenic. The employment of the latter drug in animals (horses) in order to give them a pleasing plumpness, is likewise well known.

The causal factor of an improper nutrition is not only related to the following, but might be brought into direct connection with it.

6. *Endemic Conditions.*

The influences leading to a marked obesity and a disposition to corpulence under various climatic and endemic conditions, customs, and habits, are always those whose effect and *modus operandi* have been explained above.

Under the hot sun of southern climates the combustion of fat is most restricted with regard to the production of heat; therefore a diet which is just sufficient for the needs of the body in a temperate zone will lead to the deposition of fat, perhaps in considerable amount. The moist and warm air of the lowlands and wide plains is more favorable to corpulence than the colder air of the highlands which requires the combustion of more fat for the production of heat, and furthermore, owing to the formation of the ground, there is the necessity for greater muscular activity in climbing, as opposed to a simple walk in the plains. Accordingly we find corpulence far more frequent among the Orientals, southern Italians, Dutchmen, South Sea Islanders, etc., and also observe in them a more marked hereditary disposition to general corpulence than in those who live in northern climates and mountain regions.

Peculiar habits and customs, local modes of nutrition, and notions regarding bodily conformation and beauty frequently give rise, among people and tribes of inferior civilization, to the production of more or less extensive and sometimes frightful forms of obesity, by means of artificially forced feeding. Among the older writers it is reported by Alpin that Egyptian women consume excessive quantities of fatty drinks, especially soup made from fattened chickens always taken in connection with the flesh of a pullet, in order to acquire great obesity which they prize most highly. Poor women who are unable to afford such a luxury drink with the same object oil of sesame, oil from Indian nuts or hermodactylus, take prolonged baths in warm sweetened water, eat and drink in the bath where they also take enemas of various fats, especially that of the bear (Kisch). So also it is reported by Hesse-Wartegg that the Jewesses of Tunis when barely ten years old are systematically fattened by being confined in dark narrow rooms and fed with farinaceous articles and the flesh of young dogs,* until in the course of a few months they resemble shape-

* This must be an error; orthodox Jews are prohibited the use of the flesh of unclean animals, among which is the dog.—TRANSLATOR.

less lumps of fat. Within a like brief period Moorish women are said to attain the desired corpulence by the ingestion of a drink made from honey and a diet of fresh dates.

That such a popular method of fattening, continued for generations, may finally lead to an hereditary disposition cannot be doubted, in view of Roloff's experiments in this direction. However, we must not understand by this an endemic hereditary disposition to pronounced fat hyperplasia among a certain race of people, and we should not designate it by this term.

Symptomatology.

The external manifestations with which corpulence occurs and the order of the symptoms depend on the one hand upon the causes on which the disease rests, and on the other hand upon the stage at which it is observed. Two typical forms of corpulence, with numerous transitions, are to be observed, which differ materially, even in their earliest period, in the quality of the blood which constitutes the basis for the increased development of fat—the plethoric and the anæmic form.

Where states of the blood so diametrically opposed as in plethora and anæmia form the basis of a disease there will be differences not only in the external appearances, shape, and habits of the patient, which are largely influenced by the condition of the blood, but also in the symptoms evoked by the excessive accumulation of fat in the body, with the functional disturbances due to it—differences which can be brought into a certain contrast with each other. With the progressive development of the disease and the changes in the organism it induces the contrasts are gradually balanced as it were, the plethoric and anæmic quality of the blood being finally merged into a hydræmic quality which is merely attained earlier in persisting anæmia. The subjective and objective symptomatology then becomes more uniform, and the terminal stages of the two forms often do not permit the distinction being made as to whether they are the result of the one or the other variety.

1. Plethoric Form.

The first signs of increased fat formation and deposition in the plethoric form manifest themselves often in youth or in early manhood when the body is in the full vigor of development, and shape, carriage, and color correspond to perfect health.

With the first deposition of the excess of fat in the subcutaneous cellular tissue the limbs become rounded, gradually increase in cir-

cumference without damaging the symmetry of form; the skin everywhere is filled out by a cushion of fat and appears smooth and unwrinkled. But since with the ample or excessive nutrition and good health not only the amount of fat but also that of albumin is increased, the muscles are powerfully developed, voluminous, and capable of function as is the heart muscle; the blood generally reaches the maximum in contained albumin and hæmoglobin, and its quantity may frequently exceed the normal by a considerable degree. The external appearance of the patient fully corresponds to the state of nutrition: his face and the mucous membranes are vivid red, slightly congested; his bearing, unless the phlegmatic temperament is congenitally present or has been acquired, is self-confident and elastic; while the size and endurance of his muscles equal the normal, rarely exceed it, but more frequently are below it after the corpulence has existed a greater length of time.

In Munich there is abundant opportunity for observing such persons: the sons of rich citizens with few hours of work, who set a good table not only for the chief repasts but at various times during the day, and consume beer in large amounts, usually eight to ten litres per day, or fat-forming substances to the extent of 360–450 gm. of carbohydrates, which alone would cover or exceed their daily requirements.

On examining such patients we find in the early years a full strong pulse which later on becomes weaker, of moderate frequency, 68–72, sometimes sinking to 50–60 per minute. The area of cardiac dulness is enlarged, often considerably; the impulse is felt indistinctly, owing both to a loss of power of the heart muscle and to a greater deposit of fat on the thorax, through which the apex beat is less easily perceived. The heart sounds, at first clear and distinctly audible, subsequently lose force and are weakened by the large amounts of fat over the cardiac region. Respiration is normal. The large quantity of water ingested with the beverages is often sufficiently excreted in the urine; but not rarely several hundred cubic centimetres remain behind in the body and must be passed off in the sweat and the insensible perspiration.

At first the patients, so long as they still feel strong and are able to put forth considerable bodily power, are proud of their corpulence and imposing figure, looking down with disdain upon other less well-nourished and thin individuals, and not rarely they are the object of envy to many, not alone lean persons. Thus the person may remain for years. Later on the patient's condition changes more and more both in his external appearance and in his subjective sensations, either gradually or rapidly. The masses of fat in the

subcutaneous cellular tissue become excessive. The plumpness of the body, which before was not quite beyond the limits of symmetry, soon exceeds them, and the man who not long ago resembled a beautiful young Bacchus in shape becomes a Silenus or a Falstaff, an object of mockery.

More and more fat is deposited, obliterating the folds and furrows; the face loses its mimic expression owing to the covering and nutritive disturbances of the facial muscles by the thick layers of fat. There are persons, says Lichtenberg, who are so fat in the face that they can laugh beneath the deposit so that the greatest physiognomic expert is unable to discover it, while we poor thin creatures, whose soul lies immediately under the epidermis, are forced to speak the language of truth.

The neck appears shortened by the double chin and the fat cushions of the upper clavicular region; often an additional mass of fat in several rolls lies between the head and trunk. The chest gains in circumference, the mammary region harbors large masses of fat, and as the tenser, short-fibred connective tissue along the sternum prevents the development of the panniculus adiposus, the lateral portions in men present the appearance of female breasts, while in women the mammæ often attain an enormous bulk and finally extend down to the umbilical region as almost bag-like formations. But the largest bulk is presented by the abdomen; this is due not only to the thick external deposits but also to the interior enlargement following the distention of the internal organs, the stomach and intestinal canal, increase of volume of the liver, the mesentery, and omentum with enormous masses of fat. Thus the abdomen may attain a truly monstrous form and proportion. Its dimensions increase steadily. In thick transverse ridges, usually three, the abdomen hangs down over the thighs and covers the pubic region, while the umbilical region is drawn in in a funnel shape, and the stretching of the abdominal wall gives rise to umbilical hernia. As the weight of the abdomen brings the centre of gravity for the upright position of the body farther forward, the patients usually straddle in their walk, with legs turned outward, the head held high, the body drawn back, and with slow, careful steps like pregnant women. They also complain of pain in the back, caused by the straining of the dorsal muscles to maintain the equilibrium in walking. In the recumbent position, however, the diaphragm is pushed uncommonly high by the masses of fat accumulated in the abdomen and the enlargement of the organs by fatty infiltration, thus compressing the thoracic space which is already crowded by the enlarged fatty heart and the masses of fat in the mediastinum, oppressing the lungs and heart and causing dyspnœa

so that the patients are forced to place the head and trunk high and even to assume an almost sitting position in bed.

In the upper and lower extremities, too, the fatty deposits gradually reduce the nutrition, development, and activity of the muscles and distort the outlines. On the arm and forearm the furrows and lines limiting the muscles are filled up with fat and obliterated, the arms themselves are changed thereby into tumid cylinders the tense skin of which can no longer be lifted into folds. The thighs have still more markedly increased in bulk, especially at their upper parts, around the hips and the buttocks. At times the greatly distended cushions of fat over the tuber ischii (steatopyga of the Bushman and Hottentot women) may attain enormous proportions. On the thighs the masses of fat form several transverse ridges, while the knees exhibit but little fatty deposit and the legs again are increased in bulk by abundant adipose tissue. The deposition of fat occurs last in the hands and feet, which are often remarkably small in obesity.

After a prolonged duration of corpulence and of the various, not necessarily very pronounced, circulatory and respiratory troubles, but before the disease itself has reached its height, death may occur suddenly by paralysis of the heart. At the autopsy of such cases the terminal fatty degeneration of the heart muscle may often be absent, and the fatal issue can thus far be explained only by the assumption of a paralysis of the cardiac nerves which for the present must be called functional, until an anatomical lesion can be discovered (Bollinger). The fatigue of the heart muscle and the paralysis of the cardiac nervous system then would be due mainly to the inordinate quantity of blood and the intensity of the intracardial pressure—a fact to which I first called attention. Added to this is the influence of the lack of oxygen and the accumulation of carbonic acid in the blood which weaken the energy of cardiac activity and favor the occurrence of the paralysis.

2. Anæmic Form.

In every-day life by the side of the corpulent persons with true plethora we meet with a number of patients likewise affected with an abnormal deposition of fat in the subcutaneous cellular tissue, at the various points of predilection, and in the internal organs, but who differ materially even on superficial observation from cases of the former type.

As this difference seems to be marked by changes in the quality and quantity of the blood, by anæmia and chlorosis, it manifests it-

self mostly in early stages and decreases as the corpulence advances and with its longer duration, until hydræmic conditions gradually develop as in the plethoric form and obliterate the last distinctive mark. But the course, too, and the time in which this transition occurs differ in the two forms of obesity, and while in plethoric cases it often takes many years until the blood becomes hydræmic, this change may develop in a much shorter time, often in a few years, in anæmia and chlorosis in which the quality of the blood predisposes to it.

Instead of the florid, more congested face of the corpulent with normal blood and beginning plethora, instead of the round shape, the tensely elastic feel of the body, the but slightly diminished muscular force and general power of resistance, the full pulse and vigorous heart-beats, there are presented to us pictures which lack so many characteristic traits that they hardly seem to resemble the former. Indeed an ample deposit of fat has occurred, the face is round and full, the circumference of the chest and abdomen exceeds the normal by far, the extremities are thick, plump, and shapeless; yet the masses of fat are not tense and firm but flabby, doughy, non-resistant to pressure. The face, the external skin, and the mucous membranes are pale and anæmic; the muscles are poorly developed, flabby, and weak, usually from the beginning; the pulse is small and thin; the heart's action is lacking in force; the general energy and the power of resistance of the body are depressed. The surface of the body feels cool and the temperature is frequently subnormal. While the plethoric patient still develops much muscular power and is capable of great exertion, the strength of the anæmic corpulent patients is barely sufficient for slight daily work; they soon tire, often after slight exertion; they rapidly lose breath, suffer from palpitation, and are therefore more inclined to take it easy; they need rest, are lazy, they sleep much and long, often late in the day, and are with difficulty induced to get up. They therefore look for sedentary occupations, but without any inclination for exhausting mental activity; they avoid also in their recreations anything in the way of games and walks requiring bodily movement and muscular exertion. Nor are they as a rule great eaters. The consumption of food not rarely is below the quantity appropriate to them, and while good juicy but lean meat is taken in small amounts and with aversion, fat-forming substances, especially such as are rich in carbohydrates, constitute their chief diet. In the ingestion of fluids the patients are usually less abstemious. But it is not always alcoholic liquors, wine, beer, and whiskey, which are preferred and taken in abundance; in the majority of cases, besides coffee and tea, plain water, sugar water,

water with sweet fruit juices, lemonade, wine diluted with water form the staple drinks. Only those patients (men) whose anæmic conditions are due to the abuse of alcohol, prefer beer, wine, brandy, liqueurs, etc., and consume large quantities of these. Such patients use water but sparingly and unwillingly, frequently only when mixed with wine or brandy.

The majority of patients of this type are of the female sex: young chlorotic girls with much adipose tissue and of pale aspect. Menstruation in them is nearly always abnormal, scanty, irregular, or painful. In the same way women become corpulent who have lost much blood, have suckled children for a long time, and then have taken large amounts of unsuitable nourishment (forced feeding).

In men the anæmic form of corpulence is less apt to develop. Those in whom it does develop are usually convalescents from grave, acute wasting diseases (typhoid fever, scarlatina, articular rheumatism, cholera, pneumonia, etc.), who accumulate fat by rest, excessive and unsuitable diet; also the subjects of scrofula and a tuberculous tendency, persons suffering from pernicious anæmia, habitual drunkards, cachectic individuals, and syphilitic patients after mercurial treatment in whom a deposition of fat occurs on an anæmic basis, but who soon present the signs of a rapidly progressive hydræmia.

If we come to consider the nutrition of those patients in whom the obesity develops we find the diet to consist in the main of fat-forming substances, but the quantity is always rather small as compared to that of other persons, especially of those who work hard, who live for months almost exclusively upon fat and carbohydrates, of which they consume considerable amounts without becoming fat (woodmen, laborers in the mountain forests, etc.).

There can be no doubt that the principal cause of the abnormal accumulation of fat in these cases rests on the quality of the blood, *i.e.*, on the diminished oxidation processes in consequence of the slight hæmoglobin contents of the blood and the insufficient oxygenation dependent upon it. How greatly combustion and heat formation are reduced in the bodies of such patients can be recognized even from their low temperature which is almost without exception subnormal, with a heat deficit ranging between 0.2 and 0.5 or even 0.8° C. The diminished absorption of oxygen by the hæmoglobin and formation of oxyhæmoglobin, together with the slight oxygenation of the tissues, are associated secondarily with the insufficient nutrition and the slight functional capacity of the muscular apparatus, whose extent determines the decomposition of fat and the resulting amount of force and heat.

As we may argue a diminished decomposition of fat from the sub-

normal temperature of the body, so the quality of the muscles, their tone, their relaxed and slightly resistant condition, their small volume in the resting and contracted state, their insufficient contractile power and rapid fatigue, permit us to deduce the possible performance of work and the combustion of fat caused thereby. The early occurrence of fatigue, and the usually pre-existing shortness of breath, dyspnœa, and palpitation with any relatively greater physical exertion of such persons, *e.g.*, walking, stair-climbing, etc., are likewise signs of the slight absorption of oxygen during respiration and are proportionate to it. The oxygen absorbed by the insufficient hæmoglobin is used up by slight muscular labor. The respiratory centre is supplied with blood deficient in oxygen, and blood charged with carbonic acid becomes stagnant. The equally weak and inefficient heart muscle exhausts itself in hurried, weak, and incomplete contractions in order to propel the blood, arriving in larger amounts owing to the muscular labor, from the right heart to the lungs, but without complete success. The blood accumulates in the entire venous system, a venous hyperæmia develops even in the central organs, and produces marked irritation of the respiratory and cardiac centres.

Rapid relaxation of the muscular contractions, fatigue, and exhaustion are the immediate effects of these processes in the respiratory and circulatory apparatus, and a further result is that the patient can decompose only small quantities of fat. If such a patient takes in his food any considerable amount of fat-forming substances they will soon be no longer completely transformed and utilized, and being superfluous material they are changed into fat and deposited in the reservoirs. The patient under inferior nutrition still accumulates fat.

The accumulation of fat effected under such conditions, and with a rarely abundant ingestion of fat-forming substances and hyper-nutrition, will always be kept within certain limits which are still more restricted by the facts that the digestive apparatus, like the muscular apparatus, is impeded in its activity by the afflux of anæmic blood deficient in oxygen; that the digestion proceeds but slowly; that the craving for food, the appetite, is lessened, and that in this way not sufficient material is supplied to the body for an excessive formation of fat. In the anæmic form of obesity, therefore, the deposition of fat is never as great as in the plethoric form in which the weight may become remarkable. The quality of the fat, too, does not seem to be the same as in persons who have become plethoric by the ingestion of enormous quantities of albuminous food, fat, and carbohydrates. While the subcutaneous cellular tissue in the latter is firm and gran-

ular, elastic and hard to the touch, in anæmia it appears flaccid, soft, loose, and is readily pinched into folds.

Still another factor is of importance in the symptomatology of the anæmic corpulent persons, namely, the water. Early in this condition water accumulates in the blood and the tissues owing to the insufficiency of the heart muscle and the circulatory disturbances resulting from it. The rapid occurrence of palpitation in such patients has been already repeatedly mentioned. Even in moderate degrees of anæmic obesity palpitation of the heart, subjectively and objectively, is never absent. Vigorous, perfect contractions are lacking and are replaced by weak and rapid movements. The heart is usually dilated, and the systolic murmurs often audible over the various valves indicate the relative insufficiency, as the accentuated second pulmonary sound shows the increased pressure in the right heart and the venous apparatus. In other cases a venous hum is audible over the bulb of the internal jugular vein. At the same time the arteries are slightly filled; the pulse is small, soft, weak, and dicrotic.

The slight afflux of blood to the kidneys, and the lessened pressure of the blood in them, in their turn again influence the excretion of urine and give rise to increased tension in the other water-excreting organs, to augmented sensible and insensible perspiration, and when these are no longer sufficient, to an accumulation of water in the blood and tissues. The excretion of urine diminishes more and more. Not only is the total amount of urine small, but its excrecretion occurs also at irregular intervals; a considerable time may elapse after the ingestion of fluids before urination takes place, and then the quantity may be rather large. But finally even this irregular polyuria ceases. The water ingested within twenty-four hours in the beverages is incompletely excreted by the kidneys, leaving a very large surplus of water which can no longer be expelled from the body by the sensible and insensible perspiration. The best information on this point is gained by the determination of the differences which we shall presently discuss at greater length. These patients soon develop, beside the anæmic quality of the blood, an accumulation of water in the latter and in the tissues, hydræmia and œdemas which manifest themselves first in the lower extremities, around the ankles.

Through the co-operation of these circumstances the anæmic form of obesity passes much more rapidly into the hydræmic than does the plethoric, in which the disease may assume several phases and persist many years before the heart muscle reaches such a condition and the force of the heart sinks to the same point as it may in a few years in the anæmic form.

Sequelæ of the Organic Changes.

With the development of these changes in the various vital organs by excessive deposition of fat, conditions may result which early endanger the life of the patient, should intercurrent processes bring about additional diseases and organic changes.

The first to suffer is the muscular power, as the fat surrounds and penetrates the muscles which in part undergo fatty degeneration from the pressure and the nutritive disturbances. The strength is considerably impaired when the blood is anæmic either from the start as in the anæmic form of obesity or becomes so in the further course, so that the muscle is not supplied with sufficient oxygen.

These injurious influences gain particular importance in the heart which, as stated above, is rapidly weakened. But with the slowly increasing insufficiency of the heart muscle the general resisting power of the body, especially against intercurrent febrile diseases, sinks likewise. Observations to this effect were made even by Hippocrates, Celsus, and Galen, and in more recent times Wunderlich and Liebermeister have called special attention to the fact. The power of the heart which even in the afebrile state was able to maintain the circulation only with difficulty, is still more impaired by the fever so that the arteries are but imperfectly filled with blood; the pulse becomes small, weak, dicrotic, and irregular; and the fever assumes the adynamic character, to use the earlier term for the results of this sinking of the heart action. But in the febrile condition of such patients a further dangerous factor is superadded, to which Liebermeister has called attention. The small surface of the body of the obese as compared with his weight, in conjunction with the thick subcutaneous layer of fat, interferes with the dissipation of heat so that the temperature in the interior of the body soon reaches a high degree which damages the functions and acts deleteriously upon the heart. Hence it is not necessary to assume that the febrile diseases—typhoid fever, pneumonia, the exanthemata, etc.—in the obese are associated with an absolute higher temperature, with increased oxidation, but the greater heat in the viscera is fully explained by the retention of heat. For the same reasons—the smaller surface of the body and the enormous panniculus adiposus—it is more difficult to reduce the temperature by direct abstraction of heat, by cold baths, in the obese than in the lean; while on the other hand also the internal antipyretic drugs—antipyrin, quinine, etc.—are usually badly borne and even in moderate doses may cause a serious collapse. Corpulent persons, therefore, who are attacked by the above-named diseases are always exposed to the danger that the greater or lesser

insufficiency of the heart will rapidly increase under the fever and that a sudden collapse may terminate fatally.

Convalescence after febrile diseases in the obese also runs a slower, often an unfavorable course. Not only in pre-existing anæmia, but also in the plethoric form of obesity the hæmoglobin contents of the blood sink remarkably during the fever and the regeneration of the red corpuscles is effected with difficulty. Owing to these causes on the one hand, and on the other hand to the plentiful diet, the forced nutrition during convalescence, and the rest combined with it, there is again more fat than muscle formed, and the decomposition products of the albumin are less completely burned up and instead are changed into fat which is likewise deposited. Therefore the disturbances in the course of convalescence dependent upon cardiac weakness and anæmia will not only be greater than before, but also the corpulence will be apt to increase.

Grave dangers threaten the life of the corpulent, moreover, by the anomalies of metabolism resulting from the accumulation of fat in the body, partly by complicating diseases which either are due to the same cause as the increased fat-formation or are induced by it: uric-acid diathesis and gout, functional disturbances and diseases of the kidneys, arteriosclerosis, diabetes mellitus, carcinosis. We encounter them sooner or later in the further course of the disease. Under their baleful influence the symptomatology changes, the existing symptoms are aggravated, additional ones appear, and they determine the extent of the complicating processes which modify the termination of the disease according to their nature.

Pathological Anatomy and Pathology.

Obesity may persist in the various phases of its development for a pretty long time, with slight changes in its symptom complex, until the gradual dissolution of the organism; or else, in less frequent cases, it leads to an early fatal termination, under a rapid succession of the symptoms. Hence the changes in the various organs will differ according to the stage of the disease and its symptoms, and while the first organic changes due to the increased deposition of fat are more mechanical, degeneration will develop later on with the progress of the nutritive and circulatory disturbances.

The most conspicuous alteration in general obesity is presented by the adipose tissue and tissues inclosing fat. This alteration affects mainly the quantitative relations. The increased volume which may assume colossal dimensions; the widening, the permeation and infiltration of the substance of the different organs by fatty tissue; the

massive quantities of fat deposited in the panniculus adiposus and in the interior of the body, have already been mentioned, and when we come to the consideration of the changes in the several organs we shall revert to the proliferation of fat upon and within them. If we follow Toldt in assuming the existence of a preformed adipose tissue as an independent organ, beside the capacity of the connective-tissue cells for storing fat in hypernutrition and for changing into fat cells, we have to deal in general obesity on the one hand with an increase of the preformed adipose tissue, and on the other hand with a fatty tissue secondarily developed from the transformation of the connective-tissue cells into fat cells. The latter tissue spreads wherever connective tissue extends between the elements of the organs, especially where it penetrates from the surface. We have reason for the belief that the processes which do the most damage to the physiological functions of the vital organs are chiefly caused by the latter.

It is an empirical fact that the reduction of fat in cases of congenital obesity is effected with the utmost difficulty, often only to a limited extent, and that relapses are very frequent or form the rule; while in persons who have become corpulent only through excessive nutrition the reduction is not alone more easily attained but is also more lasting. In the latter cases we might be justified in assuming, in accordance with our presupposition, that the preformed adipose tissue does not exceed the normal and possibly may be below it, while in the former class of patients there is probably from the start an abnormally great amount of adipose tissue in which the liquefaction and combustion of the fat is brought about with greater difficulty than in a fatty tissue resulting from the absorption of fat by the connective tissue. Further anatomico-physiological investigations and experiments with reference to this theory based on empiricism, which explains many phenomena in the pathology and treatment of obesity that are otherwise hard to understand, are still lacking.

In the histological elements also quantitative differences in the accumulation of fat may be demonstrated in various cases of obesity. In the adipose tissue observed in the plethoric form, which feels elastic, tense, and hard, the fat globules are large, greatly distended, the fat cells are completely filled with fat and transformed into roundish, oval, or more elongated vesicular formations, whose membrane or nuclei can no longer be clearly recognized. The mucous or rather mucoid intermediate substance is sparsely developed, hardly demonstrable, so that the fat cells are closely packed and thus constitute a firm tissue which has a granular section even in the cadaver. In other cases of the more anæmic and hydræmic variety, with flabby, doughy masses of fat, the cells are less filled with fat,

often only half as much as the other kind, and partly contain several larger and smaller drops of fat. Membrane and nucleus are also more distinctly demonstrable. The fat globules are small, loosely put together, and the intermediate substance is more abundant, saturated with sero-mucous fluid, and imparts to the tissue the characteristic doughy quality. The tensely filled adipose tissue has a more whitish or yellowish color, in the other less completely filled fat cells the yellowish or reddish-yellow color is more pronounced. The differences in the external characteristics of the adipose tissue are due partly to the varying chemical composition of the fat, partly to the varying amount of coloring material present, and to the condition of the surrounding tissue as regards bulk and arrangement.

Aside from the cells of the adipose and connective tissue and of various organs, the fat seems also to occur in a finely divided state in some tissues and in the blood serum. Thus Valentiner found in the macroscopically normal muscles (from the centre of the pectoralis major) of three corpulent persons, hard drinkers, 3.9 to 4.9 per cent. of fat, while the same tissue from three other marasmic individuals yielded only 1.3 to 1.7 per cent. According to different observations, fat in the blood of corpulent persons can be recognized even macroscopically by the milky turbidity of the serum, but according to Becquerell and Rodier this seems to occur chiefly in drunkards.

The adipose tissue of man, which liquefies at 20 to 25° C. and solidifies below 12 to 15°, contains the glycerides of oleic and palmitic acids, with but little stearic acid; the composition changes, however, with the age of the individual. The fat of the new-born, according to Langer, contains more palmitic and stearic acids, and less oleic acid than that of the adult; its melting-point is therefore higher. But the melting-point differs also according to the organs in which the fat is deposited: it is highest in the fat of the kidney, lower in that of the subcutaneous tissue, and lowest in the fat accumulated in the liver.

Whether there is a qualitative difference in the composition of the fat in the various forms of obesity has not yet been determined, although it does not appear improbable and has even been ascribed by some authors to special etiological factors.

According to Langer's investigations the composition of the fat at different ages varies; that of the new-born contains about three times as much fatty acid, palmitic and stearic acids, as that of the adult, and he places its melting point at 45° C., while that of the adult liquefies at 36° C. Moreover, the fat of young brandy drinkers, according to Rokitansky, is said to be distinguished by an uncommon tallowy hardness and to approach in its quality some of the animal

fats such as mutton tallow. The experience of cattle breeders shows that the fat differs with the food supply, and they call it in the one case good or healthy and in the other bad or unhealthy. Quite a considerable difference in the nutrition of plethoric and anæmic corpulent persons exists also in the quantity and quality of the diet and is perpetuated in the utilization of the varying material in digestion, transformation, and deposition. There is moreover in anæmia and hydræmia a greater fat-formation by restriction of the oxidation processes in consequence of the deficiency in hæmoglobin and the accumulation of water in the blood and tissues. The experiments by Munk and others to determine the results of feeding different kinds of fat, especially mutton tallow, linseed oil, rape oil, etc., are likewise of interest in the settlement of this question.

The Blood.—The abnormal conditions of the blood in the various forms of corpulence, plethora, anæmia, and hydræmia, can be demonstrated clinically, pathologico-anatomically, and by the direct determination of the specific gravity, the hæmoglobin contents, the density, and the proportion of water.

Although we have no figures in proof of a true plethora, yet clinical and anatomical facts point indisputably to the presence of such a quantitative anomaly of the blood. Individuals in whom we are forced to assume the existence of plethora have, as shown in the symptomatology, a full, strong, tense pulse, a pronounced disposition to congestions, exhibit hyperæmia of the external skin and the mucous membranes, a marked tendency to hemorrhages, especially in the brain and lungs, by reason of greater or lesser rise of blood pressure. At the autopsy we find a considerable amount of blood, together with hypertrophy and dilatation of the heart in consequence of the persistently increased demands upon it; while the circulatory apparatus is under an abnormally high tension, even when the increased amount of blood is compensated for by enlargement of the heart (dilatation). Hence we find in the entire vascular apparatus clear evidence of a larger mass of blood which fills it, and it should be especially noted that the blood-vessels, like the heart, adapt themselves to the volume of the blood. In plethoric persons the vessels are greatly dilated as far as the capillaries, and their walls are thickened, while in chronic anæmia they appear narrowly contracted and thin-walled. The differences are most marked in the thickness of the wall and the width of the aorta, which in the plethoric is found three or four times as wide as in the anæmic.

The specific gravity of the entire blood shows an increase to and beyond 1.066 and 1.068, and that of the serum up to 1.033 and 1.034. The hæmoglobin contents may rise beyond 106 per cent. Higher

percentages, beyond 108 and 110, are doubtless due to congestive concentration. The coefficient of density at the same time will likewise indicate 100 to 105, as determined with Bizzozero's cytometer. In anæmia the specific gravity sinks to 1.057–1.058 and often lower, the serum reaches at most 1.028, while the hæmoglobin contents may amount to 80 per cent. and less. The coefficient of density may fall to 70 and even less. In women all these figures are much lower, corresponding to the general proportions of their blood as compared with that of man. In plethora the specific gravity of the entire blood is at most 1.062, that of the serum 1.029, hæmoglobin contents 90 per cent., coefficient of density 90–95. The lowest figures I found in anæmia were: specific gravity of the entire blood 1.050, that of the serum 1.021, hæmoglobin contents 64 per cent., coefficient of density 67.8.

As compared with true plethora we find here an overfilling of the vascular apparatus with a blood which no longer possesses the normal composition, but shows more or less marked deviations as regards a diminution of its solid constituents and an increase of water.

Serous plethora develops chiefly when the excretion of the superfluous water is interfered with by disturbances of the cardiac and renal activity. Owing to the accumulation of water in the blood, despite the existing absolute hypalbuminosis, the volume of the blood is augmented and the vascular apparatus is abnormally filled, at least temporarily until hydropic excretion occurs. Hence as a rule the contrast between the pallor of the face, of the external skin, and the mucous membranes of such persons on the one hand, and on the other the fulness of the vascular apparatus (abnormally high tension of the pulse) is striking. At the autopsy of such obese persons the internal organs are usually remarkably deficient in normally colored blood, as compared to the above-described findings in true plethora, and generally filled with only a small amount of pale, loosely coagulated blood (v. Recklinghausen).

In pronounced forms of hydræmia, according to the older observations, the amount of albumin in the blood is as a rule below 60 per cent. (Becquerel and Rodier, Andrea and Gavaret, Abeille, C. Schmitt, and others), while the salts dissolved in the plasma remain behind with the retained water; according to C. Schmitt in the proportion of nine parts of plasma albumin to one part of the ordinary plasma salts. The specific gravity of the entire blood, according to my observations, is in men 1.057, that of the serum 1.023, hæmoglobin contents 83 per cent., coefficient of density 80. In women I obtained as extreme values: specific gravity of the entire blood 1.043, that of the serum 1.019, hæmoglobin contents 45–50 per cent., coefficient of density 56.

The Arteries.—Changes in the vascular apparatus proper develop among the older corpulent persons as a rule with the symptoms of chronic endarteritis—opacity, thickening and softening of the intima with partial fatty metamorphosis of the latter; these changes may occasionally extend to the media and adventitia, and by the deposition of lime salts, etc., lead to the complicating diseases, sclerosis and atheroma.

In the anæmic type of corpulence, among girls, women, and young persons, the anatomical changes in the arteries are limited to the simple fatty degeneration of the intima and media peculiar to anæmia, and may be often entirely absent in early age. As regards the venous system, special mention must be made of the occurrence of varices on the legs, hemorrhoidal nodules about the rectum, varicocele, etc., mainly in patients with plethora and in advanced age (see below).

The Heart.—The heart muscle, as long as but little fat covers it, will be able to respond to the increased demands, often even for a long time, or it hypertrophies under moderate dilatation of its cavities, corresponding to the greater quantity of blood, as it does in pregnancy in which it answers similar requirements.* The patient suffers no or but inconsiderable inconveniences, perhaps only after active exertions such as running and stair-climbing, especially after a more or less ample meal when the thoracic space is at the same time diminished by the upward movement of the diaphragm. In some cases shortness of breath and palpitation set in after a full meal. Other symptoms on the part of the respiratory apparatus are still absent. Physical examination shows either normal conditions or at most slight enlargement of the area of cardiac dulness; the apex beat is somewhat displaced outward, the sounds are pure, but slightly muffled according to the more or less thick interposition of the fatty deposit.

Only when with the gradual augmentation of fat the deposit on the heart is likewise increased, especially when the fat accumulates more and more beneath the pericardium, begins to penetrate from the sulci between the muscular layers, and the structure becomes looser, do the muscular walls distend—first the left heart by reason of the resistance in the greater arterial system and the steadily rising intracardial pressure—and a dilatation of the left ventricle results which leads to its hypertrophy. Since a compensation of the advancing disturbances in the circulatory apparatus is not effected

* In this case hypertrophy and dilatation must still be considered as phenomena of growth and invigoration.

thereby, or is so for a short time only, and the left heart is unable to dispose completely of the increased amount of blood which flows into it, the blood stagnates in the left auricle and dilates it, and regurgitates and accumulates in the lungs, which in their turn increase the work of the right heart, and when the latter is unable to respond to it, a dilatation and hypertrophy of the right ventricle will be superadded. But this lesion of the circulatory apparatus is not final. The right ventricle is less able than the left to effect compensation, and hence the congestion continues in the right auricle and the venous apparatus back of it, causing dilatation and overfilling of its vessels. It is obvious that this condition will result sooner in proportion as the heart is unable to resist the on-flowing blood masses and the ever-increasing intracardial pressure, that is to say, the greater the deposition and penetration of the fat upon and into the muscle the more rapid the progress of the lesion. On the other hand, the resistance in the vascular apparatus by the accumulation of fat in the body, the viscera, and tissues, is increased by the fact that the fatty deposits hinder the dilatation of the arterial tube and prevent a rapid transition of the arterial systole into the diastole. The fatty deposits and the compression of the arteries therefore influence at the same time the movements of the heart and the pulse, which latter assumes the character of the pulsus tardus as the heart slowly surmounts the obstacles present in addition to the delayed expansion and contraction of the arteries.

Percussion shows the area of cardiac dulness enlarged, according to the stage of the fatty heart, first in length, later also in width. A larger portion of the heart adjoins the thoracic wall, the impulse is diffuse and lacks force, and the apex beat is usually displaced outward, possesses slight resistance, and often cannot be felt.

On auscultation the heart sounds are clear when no complication is present; when the hypertrophy and dilatation are still confined mainly to the left heart they are loud and distinct, frequently with accentuation of the second aortic sound. But when the signs of insufficiency of the left ventricle become more marked and the right ventricle has likewise undergone dilatation and hypertrophy, then the heart sounds diminish in intensity, they become muffled with ever more distinct accentuation of the second pulmonic sound. A reduplicated sound may also be observed in systole owing to the unequal contraction of the ventricles.

The pulse in the majority of cases is slow (pulsus tardus), especially when the obesity is great and plethora exists. In other cases it becomes frequent and may lose in quality with the progress of the circulatory disturbances, until it finally is dicrotic or subdicrotic.

At the same time with the increasing weakness of the heart the impeded circulation becomes perceptible by reason of regurgitation of the blood in the venous apparatus, and dilatation of the smaller cutaneous veins; we see this, for instance, in the circle of ectatic veins and capillaries which start from the ensiform process and extend along the lower margin of the ribs toward both sides, also by the formation of varices on the extremities and dilatation of the rectal veins which are most apt to exhibit the influence of gravity and the slight propulsive and aspirating force of the heart. The rectal veins are not only dependent in every normal position of the body, but the efflux of the blood is besides frequently impeded by fæcal accumulations at the upper part of the rectum, due to the excessive and improper nutrition.

The symptoms of the patient will be intensified more or less rapidly according to the increase of the circulatory disturbances, which are compensated less and less completely by the fatty heart; embarrassed respiration, shortness of breath, and palpitation will occur even on moderate exertion such as a quick walk and stair-climbing, and will reach a distressing height with more violent efforts. Not rarely there may be frequent attacks of dyspnœa and vertigo. When the obesity has attained a high degree the patients are nearly always forced, after a short walk or ascent, often after every few steps, to stop and breathe with open mouth and distended nostrils, to gasp for air. At the same time the excitement of the heart has risen to a violent palpitation, and the storm is allayed, the respiration becoming freer and deeper, only when the patient remains standing and keeps perfectly quiet. Any at all active muscular exertion, movement of the arms, turning of the head, stooping or sitting down, during which the abdominal viscera are crowded upward and the respiratory space is contracted, immediately increases the dyspnœa and palpitation, and forces the patient to rise. Often prolonged absolute rest is necessary before normal respiration and cardiac action are restored.

Respiratory Apparatus.—The respiratory symptoms of such patients are due not only to the insufficiency of the heart muscle and the overfilling of the lungs by reason of the regurgitation of the blood, but they are also increased by the mechanical influence of the masses of fat accumulated in the body. The large abdominal deposits of fat crowd the diaphragm far up into the thoracic space and diminish its capacity, while the enlarged and not rarely great volume of the fatty heart and the fat accumulated in the mediastinum lessen it still more. Moreover the fat on the surface of the thorax, which is not rarely enormous, influences the respiratory space, since the

weak, fatty, impotent muscles are unable to lift and distend the thoracic walls, with their heavy load, in a normal manner; and on the other hand the diaphragm cannot force down, as under ordinary conditions, the elevated abdominal viscera, enlarged as they are by fatty infiltration and deposition, into the abdomen which is likewise burdened with thick, almost unyielding deposits of fat. Hence the respiratory capacity of the lungs and their inspiratory distention are considerably restricted from two sides. This explains why even at this stage, without further pathological alterations in the heart and lungs, the patients quickly become short of breath at night, especially when low down in the bed, as the abdominal viscera then gravitate farther into the thorax; or why they lose breath when the stomach is greatly distended; or finally why the dyspnœic symptoms, which may assume the character of asthmatic attacks, wake the patient and cause him to sit up or jump out of bed.

The weak heart action, the stasis in the venous apparatus, and the slight excursive power of the thorax gradually cause in the bronchial mucosa and in the compressed lungs an extensive congestive hyperæmia which in its turn gives rise to catarrhs with nearly uniformly chronic course and frequent acute exacerbations, either spontaneously or after slight irritation such as change of temperature, inspiration of cold air, stay in damp rooms, wind, a wetting, etc. The patients cough much, expectorate continually, the breathing of any at all irritating air may produce paroxysms of cough, or the mucus accumulated in the bronchi may give rise to it. While the percussion sound of the lung is proportionately weakened by the increasing layer of fat, we perceive in auscultation, aside from a more or less altered, exaggerated, or diminished vesicular murmur, various small and large vesicular râles, purring and whistling sounds over larger or smaller portions of the lungs. In these ever acutely exacerbating chronic catarrhs lies the further danger to the patient of a lobular catarrhal pneumonia, as the inflammation readily extends from the bronchi to the alveoli, even by the irritation of the trickling or aspirated mucus. Owing to the insufficiency of the heart muscle the prognosis of such pneumonias in the obese is as a rule unfavorable and a fatal termination is rather frequent.

Further results of the chronic catarrhs of the air passages, owing to the high expiratory pressure in the paroxysms of cough and to the distention of the alveoli whose bronchioles are plugged by swelling and mucus during the forced inspiration, are inflation of the lung tissue, diminution of its elasticity, and emphysema, which latter again leads to disturbances in the pulmonary circulation and adds another complication to the disease.

Influence of the Circulatory Disturbances upon the Excretion of Water by the Skin and Kidneys.—The irritability of the sweat glands and the secretion of sweat which is dependent upon heat, muscular activity, and nervous influences, is greatly increased in corpulence. The skin is congested, the sweat glands are in a state of continual irritation, and the insensible perspiration is increased. A barely appreciable rise of temperature, and the least apparent exertion, but which in the corpulent, owing to the displacement of the heavy masses of fat deposited on the body, is always associated with considerable muscular effort and leads to increased manifestation of energy and development of heat, cause more or less profuse sweating. The augmented excretion of water by the skin, however, is due also to another cause, namely, the lessened excretion of water by the kidneys, which becomes more and more perceptible with the increase of the circulatory disturbances and the stasis in the venous apparatus, and is followed by greater tension in the vicariously acting organs, the skin and lungs. In this stage the quantity of urine during twenty-four hours varies between 600 and 1,500 c.c. (20 and 50 ounces), of course according to the amount of fluid ingested.

If the amounts of fluid ingested and of urine excreted during twenty-four hours are carefully measured in such patients and the difference noted, most remarkable results are often obtained. Under ordinary nutritive conditions and an average amount of water in the solid food, the kidneys excrete normally, unless special causes are present for increased excretion of water by the skin and lungs, about 18 to 30 per cent. less than the water ingested with the beverages. This difference, together with the water contained in the solids, passes off in the sensible and insensible perspiration. Instead of this nearly constant difference, we obtain in these patients a deficit sometimes of 40 to 60 per cent., sometimes of only 5 to 10 per cent.—even making allowance for the perspiration or preventing it as much as possible—or sometimes a surplus in the urine of from 6 to 10 per cent. and more. Allowing in this calculation for the water normally excreted by the skin, 18 to 30 per cent., we have a surplus of 36 to 40 per cent. which can only be derived from the water accumulated in the body.

Hence quite marked irregularities in the urinary secretion are manifested, which occur in the form of polyuria and oliguria, the former of which always removes more or less completely the water left in the body by the latter. In the further course of the circulatory disturbances these relations change, but always more and more to the disadvantage of the excretion of water by the kidneys. The polyurias occur more rarely and no longer deplete the blood and the

tissues sufficiently of the water accumulated in them, and the plethoric form of corpulence gradually changes into the hydræmic.

The urine varies in concentration according to the quantity passed. When the conditions are still normal it hardly differs from the ordinary. In oliguria it is highly colored, dark yellow, brown to dark brown, and on cooling deposits a large quantity of urates. But when polyuria occurs the coloring matter is more diluted by the large amount of excreted water and the urine appears lighter, pale yellow or almost colorless. The specific gravity depends altogether on the concentration of the urine. Of the solid constituents the quantity of urea varies according to the ingestion of nitrogen and its transformation in the body. The urates and uric acid are most frequently increased and form the chief constituents of the sediment. But an excretion of large amounts of oxalic acid and even true oxaluria may be observed.

The overloading of the urine with urates and uric acid, which are still further increased by the frequent complication of obesity with the uric-acid diathesis and gout, leads to the development of concretions in the urinary passages, in the pelvis of the kidney, and in the bladder, and adds to the discomfort of the patients. The stones consist mainly of urates and free uric acid, more rarely of oxalic acid and phosphates.

The liver of the patients is not only influenced by the chronic hyperæmia which by itself may lead to swelling and enlargement, but has absorbed in its cells large masses of fat in consequence of the excessive fat-formation in the body, and hence presents usually a very considerable increase, especially in thickness, while the anterior margin has lost its sharpness and has become rounded and tumid.

The enlargement of the liver can be easily demonstrated by percussion, owing to the thickening and the sharper demarcation of the lower margin, especially on percussing from the abdomen upward, when the liver dulness begins farther down below the ribs; but a marked enlargement upward is rarely found. The resistance of the liver can be less readily felt on palpation by reason of the thickened abdominal walls. The liver is not painful on pressure and causes no other notable symptoms. The patients are inconvenienced chiefly when they lie on the left side, as the bulky liver, which sinks down from its great weight and presses on the remaining organs, interferes with quiet sleep.

The secretion of bile by the liver is not disturbed by the excessive absorption of fat. Not very rarely, however, the outflow of bile may be impeded, and the incarceration of gall-stones in the bile ducts may cause painful attacks of colic.

With an abundant consumption of alcohol the fatty liver may early present symptoms of degeneration, and cirrhosis may develop so that the organ is found smaller than normal. The chronic diarrhœas observed in corpulent persons should be ascribed, according to Kisch, rather to the alcoholism than to the fatty degeneration of the liver, since the latter condition is generally associated with habitual constipation.

Stomach and Intestinal Canal.—In the early years of obesity, in the great majority of cases, nutrition is excessive, often enormous quantities of solid and liquid, suitable and unsuitable foods and drinks being consumed.

By the overloading with, as a rule, very indigestible substances the stomach is dilated, gastrectasia results, with abnormally long retention of the contents. Associated with this condition are dyspepsias and gastric catarrhs of various kinds, partly due to the insult by the inappropriate nutrition, partly to the circulatory disturbances in the portal system. The plentiful meals are followed by sour eructations, heartburn, or extensive development of gases which may produce a more or less troublesome distention of the stomach and tympanites. Only after several painful hours larger masses of slightly odorous gases pass by the intestine and in a short time ease the patient. However, the gases escaping upward and downward may also often acquire a very offensive quality from the retained ingesta. Smaller quantities of gas are frequently expelled by vigorous peristaltic movements, when a rumbling, gurgling noise may be heard at a distance.

Another, but on the whole rare, symptom is the occasional sensation of boulimia. In this condition the patients not only consume during the day the usual and perhaps more than ample meals, but they are obliged, when the attacks occur, to ingest additional and large amounts of the most heterogeneous and bulky foods; even at night the patients are awakened from sleep by a sensation of hunger and eat considerable quantities of bread, meat, eggs, etc. Extensive dilatation of the stomach is seldom absent under such conditions.

Much more frequently than boulimia, a sensation of thirst comes into the foreground in the course of obesity. Great eaters are usually also great drinkers. The consumption of large quantities of food, much of which is spiced, sharp, and thirst-producing, likewise calls for increased ingestion of fluids, and when the thirst is once thoroughly aroused it can hardly be quenched by ever so large amounts of liquids. Besides, the strongly spiced dishes lead to chronic catarrhs of the oral and pharyngeal cavities (pharyngitis sicca) which are associated with altered secretion and dryness of the

mucous membranes. With the gradually developed dyspepsia, however, the appetite is lost and the craving for drink becomes the more imperative and unquenchable. The patients at last eat very little but consume instead quite incredible quantities of fluids, even plain water.

But should much alcohol be ingested with the other liquids, or should strong alcoholic liquors be chiefly consumed, the gravest forms of dyspepsia set in. The gastric mucosa which is altered by the congestive catarrhs, and the food in the process of digestion, are particularly acted upon by the alcohol in an unfavorable manner and the progress of digestion is retarded.

The first damage suffered by the intestine and its functions through the ingestion of large quantities of food consists likewise in distention by the bulk of its contents and by the gases resulting from the abnormal decompositions, and in an impeded peristalsis. The intestine is unable to propel the great masses in an adequate manner, it becomes ectatic, constipation and obstruction follow, and in their turn cause intestinal irritation with frequent thin-fluid evacuations which, however, do not remove the bulk of the hardened fæces. In the presence of diarrhœa the patients complain of insufficient evacuation and constipation, of pressure on the chest, difficult respiration, and palpitation of the heart; they feel psychically out of sorts and resemble hypochondriacal sufferers from hemorrhoids. A phlegmatic temperament, slight bodily activity, and a sedentary occupation or mode of life particularly favor the abdominal disturbances. A true inflammation may also result from the constipation, especially in the cæcum in which the fæces remain the longest and in the surrounding structures, namely, typhlitis and perityphlitis, which are apt to assume a serious character and end fatally.

Should a catarrhal inflammation develop in the intestinal mucous membrane from the constipation, the latter is soon followed by chronic diarrhœa, which is also frequent in obesity associated with alcoholism.

The last mechanical effect of the accumulation of fat in the abdominal cavity to be mentioned is the formation of fat hernias and necrosis. The hernias owe their origin to the proliferation of fat into a hernial sac, vascular opening, or into fissures of the abdominal wall whose tissues have separated here and there under the high pressure of the viscera, most frequently in the linea alba between the umbilicus and the ensiform process, more rarely above the symphysis. After the reposition of the soft, easily reducible but painful tumors the opening in the linea alba through which they have escaped can be distinctly felt. Should the fatty tumors situated outside of the peritoneum drag the latter along like a blind sac, true

hernias may result. The same cause, the slight resistance of the abdominal walls, may also give rise to true abdominal hernias, especially umbilical hernias, which of course are more frequent in women than in men. When hernias are present in connection with constipation the penetrating fæces may cause incarceration, which always leads to dangerous complications by reason of the thick superincumbent masses of fat.

In the adipose tissue, especially that proliferating between the glandular lobules of the pancreas and its surroundings, there has been observed, first by Balser, then by Ponfick, Klob, and Chiari, a circumscribed necrosis, fat necrosis, which develops in patches without inflammation. At other points, too, in the mesenteric adipose tissue, in the omental bursa, in the subpericardial and subpleural adipose tissue, also in the panniculus adiposus and in the bone marrow, opaque yellowish-white patches were found, which were punctiform or from the size of a pin-head to that of a pea; some of them could be enucleated or were softened and doughy, others were undergoing calcification. They produced no symptoms recognizable during life. Whether glycosuria was present with the disease of the pancreas was not stated; probably no attention was paid to it. Chiari considers this necrosis as a concomitant phenomenon of a grave marasmus, as he found it present only in connection with serious diseases of the body (*cf.* section on diabetes mellitus).

Sexual Organs.—The sexual organs also suffer from the excessive accumulation of fat in the body. Even the mechanical influence of the enormous masses of fat with the associated circulatory anomalies must exert a similar influence upon the sexual organs as upon other viscera, and produce disturbances which prejudice their nutrition, development, and function as well as sexual life in general.

First we must mention the diminution of the copulative capacity and fertility. The large masses of fat on the abdomen in man may obstruct coition, and prevent it even when obesity is not present in both sexes. But the virility and the sexual appetite of men likewise decrease. The semen of such individuals contains remarkable few or almost immobile spermatozoa. Azoospermia is not rarely present. In some regions of the Orient where the men are remarkable for their obesity male impotence is said to be truly endemic.

In women the deposition of excessive masses of fat causes on the external sexual organs, the breasts and the vulva, changes of form, increased volume, and tumefactions which by their mere bulk partly destroy the symmetry, partly give rise to numerous inconveniences.

The breasts, in a few rare cases, may reach an enormous size by the excessive development of fat. Kisch describes a breast meas-

uring 31 cm. in length and 60 cm. in circumference. Portalupi removed a breast weighing 52 lbs., and from a woman aged twenty-one years Robert and Amussat extirpated the mammæ which weighed respectively 30½ and 20½ lbs. Such breasts require special supporting apparatus in the erect and recumbent positions, etc. Then the pressure, friction, and sweat cause, especially at the folds under the breast and at their inner surface, erythema, excoriation of the skin, eczema, and intertrigo which are apt to become painful and heal with difficulty.

At the vulva the labia majora and minora may appear more or less enlarged by deposits of fat, or tumors may develop on them or on other parts whereby urination is interfered with and inflammatory alterations are produced in the skin at the inner surface of the labia, which are increased by the hypersecretion of the usually coexistent inflammation of the vaginal mucosa. Owing to the difficult or neglected cleansing of the parts, erythema, eczema, pruritus, inflammation of the hair and sebaceous follicles of the labia majora, and numerous small furuncles appear, while at the same time the skin of the upper and inner surface of the thighs is excoriated and inflamed by the escaping secretion, the sweat, and the friction.

The internal organs also suffer by the pressure, displacement, stretching, and dragging caused by the masses of fat in the abdomen and pelvis, by the intestines filled with ingesta of various kinds, and the frequent constipation; they are further influenced by the impeded circulation in the portal system, by the arterial anæmia and venous hyperæmia, which give rise to nutritive disturbances, hypersecretion, inflammatory processes, and exudations.

Hence on the one hand displacement of the uterus, anteflexion and retroflexion, anteversion, and prolapsus of the uterus and vagina, and on the other hand menstrual anomalies, amenorrhœa, scanty menstruation, metrorrhagia, chronic metritis, and leucorrhœa constitute frequent diseases among corpulent girls and women. The sterility of such women is mainly due to these morbid conditions which explain the fact observed already by Hippocrates that the obesity of women—as an instance he cites the women of the Scythians—is the cause of their sterility.

Lastly the frequent occurrence of abortion in corpulent women is connected with the crowded space of the pelvis and abdomen in which the pregnant uterus cannot enlarge. The effect of the masses of fat is the same as that of other abdominal tumors which lead to abortion by the crowding and pressure.

The Skin.—Among the organic diseases mention should be made of some symptoms presented by the skin.

The increased secretion of sweat has been already referred to. It is largely connected with the circulatory disturbances dependent upon the insufficiency of the heart muscle and the augmented heat production. But the sebaceous glands of the skin are also overactive, and the fatty and oily secretion elaborated by them in large amounts spreads over the surface of the skin, especially that of the face, and gives it a shining appearance. Withal the sebaceous glands are usually filled with secretion which can be expressed in the shape of soft white plugs, or when thicker is retained in the glands and forms millet-seed to hemp-seed sized nodules, comedones, in the centre of which a dirty-gray or black point marks the efferent duct of the gland.

The increased secretion of the sweat and sebaceous glands causes at various parts of the body where two cutaneous surfaces come in contact—on the neck, in the axillæ, under the female breast, at the umbilicus, at the folds of the abdomen and the inguinal region, on the scrotum and the labia, on the inner surface of the thighs, which are kept moist by the perspiration and the sebaceous secretion—maceration of the epidermis and, by the friction, hyperæmia, excoriation, and intertrigo.

Other well-known diseases of the skin in obesity are furunculosis and the formation of caruncles, while with the abuse of alcohol, and sometimes in women about the menopause, acne rosacea is of common occurrence.

As regards the hair, both hypertrichosis and alopecia occur in corpulence. The excessive growth of hair then extends also to those parts where, in accordance with the age or sex, no hair or at most lanugo is normally present: in women on the upper lip, chin, and cheeks, or on the breast, back, arms, and thighs. In the majority of cases, however, we may observe a deficient growth of the hair and beard, or an entire absence of the beard and premature baldness, as well as falling of the hair on other parts of the body such as the genitals.

Further Course of the Disease; Complications and Termination.

Even at a more advanced stage of the disease obesity may persist for years almost unchanged, differing individually by the preponderance of one or another symptom. The patients may perhaps reach a great age and death result from an intercurrent disease. In the majority of cases the malady advances with a gradual alteration of the subjective and objective symptoms and not rarely with a proportionate increase of the inconveniences.

While in the early stages the disturbances were chiefly mechanical, due to the masses of fat accumulated in the body, later on degenerative processes develop by degrees in the various organs and influence the symptomatology more or less in accordance with them.

The blood suffers soonest by the prevailing nutritive disturbances. At first its hæmoglobin contents diminish slowly but steadily, and with the increasing irregularities in the excretion of water by the urine and the invariably abundant ingestion of fluids the composition of the blood alters also in other ways. The specific gravity by degrees becomes more and more variable, reaching the lowest point of the normal limit and finally sinking below it, while the specific gravity of the serum is often before that time found subnormal. The plethoric character is lost and the blood approaches more or less rapidly a condition of anæmia and hydræmia until the obesity has changed completely into the hydræmic form. Owing to the diminution of the hæmoglobin in the blood the oxidation processes are first reduced, as is the case from the start in the anæmic form; the fat-forming substances are less perfectly burned up and are more largely deposited as fat. Since in progressive obesity, as stated above, the appetite often lessens, fat may be continually deposited even in cases in which the ingestion of fat and carbohydrates is not very great.

On the heart the fatty deposits increase steadily, spread from the sulci farther and farther over the surface, and penetrate between the muscular bundles into the substance of the organ. Under the pressure of the growing masses of fat the nutrition of the heart muscle suffers, the fibres atrophy in part or undergo fatty degeneration; the power of resistance of the muscle against the rising intracardial pressure decreases, the existing dilatation increases, and owing to the nutritive disturbances present the compensatory hypertrophy no longer suffices. Thus the heart becomes gradually less able to respond to the demands made upon its function. Besides, the lack of oxygen in the blood, as in the anæmic form, influences the restitution of the inogen decomposed by the contractions, and reduces the capacity not only of the voluntary muscles but also, and especially, that of the heart muscle.

The contractions of the heart become ever less energetic, the weak impulse cannot be felt, the heart sounds are faint and often barely perceptible; the pulse is small, thin, frequent, and traces dicrotic and subdicrotic curves. The heart strives to make up for the loss of power and amplitude of the contractions by increasing their number so as to propel the blood. In this way the work of the heart becomes ever less efficient. The arteries are filled less and the stagnation in the venous apparatus increases. Arterial anæmia and venous hyper-

æmia form constant symptoms. With the increasing weakness of the heart the organ also presents greater irritability manifested by irregularities in its movements—alternate accentuated contractions and palpitations proceeding even to stormy heart action—either spontaneously produced, *i.e.*, without demonstrable external agency, or from insignificant causes such as slight physical exertion, excitement, etc. The arterial anæmia and the lack of hæmoglobin in the blood on the other hand are bound to lead to marked disturbances in the respiratory apparatus, shortness of breath and dyspnœa, which are increased still more by the restricted thoracic movements, the shallow inspirations.

Cardiac Asthma.—When the insufficiency of the heart muscle is neither total nor constant, but is partial and temporary, confined to the left heart while the right ventricle is still capable of relatively vigorous contractions, we meet with grave paroxysmal respiratory and circulatory disturbances—cardiac asthma. The attacks usually occur at night, when the respiration during sleep has become more superficial, the rima glottidis narrower, and the tension of the oxygen in the lungs and blood has greatly decreased. The contractions of the left ventricle become progressively weaker and more incomplete, less and less blood flows into the arteries, while the right heart still pumps its contents into the lungs. The latter are more and more filled with blood, they lose their elasticity, grow rigid, the respiratory expansion and contraction become ever more incomplete, the insufficiency extends equally to inspiration and expiration. The patient awakes with oppression and pain in the chest, gasps for air, is forced to sit up or leave the bed, lips and cheeks are cyanotic, cold sweat bedews face and chest, and respiration is labored, all the auxiliary respiratory muscles being called in play. Despite the insufficiency of the heart muscle the blood pressure may rise in the arteries owing to the dyspnœa and the vascular spasm dependent upon it, and will sink only in grave cases in which the insufficiency of the heart is greater than the irritability of the vasomotor nerves.

The expectoration in such cases is always scanty. According to the condition of the bronchial mucosa, small, tough, dirty-gray or more yellowish masses, rarely mixed with blood, are coughed up, while numerous small vesicular râles are heard scattered over the chest, and along with them partly vesicular, partly rough and obscure breathing. The attacks of cardiac asthma may occur, though rarely, in the early stage of corpulence, are always a symptom of marked weakness of the heart, and appear chiefly and reach a most painful and serious character when more or less extensive degenerative processes have been established in the heart and the arteries, or when

the arterial sclerosis is latent and can be inferred only from the high blood pressure.

With the gradual weakening of the heart muscle and the fall of the pressure in the aortic system, the excretion of water by the kidneys will also undergo increasing changes which manifest themselves by scanty and irregular, or again by profuse, secretion of urine.

On comparing the quantities of water ingested in drinks and otherwise, which are usually exceedingly great, with the excretion of urine during twenty-four hours, preventing as far as possible all perspiration, we find a great deficit, 40 to 60 per cent., not rarely 1,000 to 1,500 c.c., so that, making allowance for the water contained in the solid food, it can no longer be completely removed from the body by the sensible and insensible perspiration. A portion of the ingested water remains in the body and the tissues, rendering them succulent and watery, and imparts to the patient the bloated, flaccid appearance which strikes one all the more because of the anæmic pallor and cyanosis, and contrasts strongly with the earlier elastic firmness of the body. Marked partial dropsies and œdemas do not occur at first, as the accumulated water can still escape by the occasional polyurias. If the ingestion of fluids in such a patient is restricted to 750 or 1,000 or 1,200 c.c., according to the bulk of the body and the quantity of liquids previously consumed, the excretion of urine is materially increased so that not only much more urine is passed than the amount of fluids ingested, but often enough the quantity of urine is absolutely greater than that excreted under ample or abundant consumption of fluids. As a rule the excretion of urine remains for a long time inversely proportional to the ingestion of fluids, and altogether more urine is passed than the amount of fluids consumed. The secretion of urine is greater, and in this case the excess, when the body can furnish no more fluid, is accounted for by the diminution of the excretion through the skin, which gradually becomes very much less.

Arteriosclerosis.—A frequent and grave complication of obesity, which occurs sooner or later, is the decrease in the elasticity of the vascular walls and the lessening of the contractility of their smooth muscular fibres, with increase in the thickness of the walls—sclerosis of the arteries, especially of the coronary arteries of the heart.

It is not positively proved that the obesity causes the arterial sclerosis (Traube and Huchard) especially through the high blood pressure, which is kept up by the impeded circulation in the abdominal vessels and the portal system, although persistent high blood pressure does impair the elasticity of the vascular walls and give rise to sclerosing processes. The same causes which lead to obesity—the

excessive nutrition, the ingestion of large quantities of food and drink, especially the abuse of alcohol—will also favor the occurrence of sclerosis; and mental strain and emotions, sexual excesses, the abuse of tobacco, rheumatism, gout, and the climacteric constitute additional etiological factors.

Arteriosclerosis manifests itself at an early period clinically by remarkably high tension of the pulse. The blood pressure in the radial artery, whose wall possibly shows as yet no anatomical alterations, frequently reaches 150 mm. of mercury and may exceed it; rarely it remains below this figure. Subjective symptoms may at that time be lacking. Later on difficult respiration and slight dyspnœa occur after insignificant muscular exertion, stair-climbing, stooping, etc. No changes are as yet to be noticed in the heart. The area of cardiac dulness is enlarged, the apex beat, whether palpable or not, is lower down and displaced within the mammillary line, the heart sounds are more or less muffled, or clear, and only the second aortic sound is accentuated. The pulse tracing shows no changes except high pressure. Subsequently, under the increasing pressure, the arteries become elongated and serpentine, their walls thicken and grow rigid. When the fat on the arm is thick these alterations are not distinctly perceptible in the radial artery. The temporal artery likewise, when imbedded in fat, may escape simple observation, but projects at once above the level of the temple and the forehead when these parts are rubbed with the finger, a piece of chamois or glove leather, or a handkerchief, and clearly shows its elongation and serpentine course.

With the rise in the peripheral resistance in the arterial system the force of the heart is usually increased, at first by compensatory hypertrophy of its muscle, so that the circulation is not notably disturbed. In the further course, with augmenting fat deposition and penetration of the heart muscle, pressure, atrophy, and partial fatty degeneration, and also with increasing loss of oxygen of the blood and its influence upon the inogen of the muscle fibres, the capacity of the heart again diminishes and a fresh noxious factor is added when the sclerosing process extends to the coronary arteries. By the thickening of the arterial wall the nutrition of the muscles suffers more and more, and destructive processes and atrophying degeneration become more extensive so that the heart yields further to the intracardial pressure and undergoes dilatation which is compensated with difficulty or not at all. Then symptoms of fatigue of the heart gradually appear. The contractions intermit, at first in longer, later in shorter pauses, thus showing by degrees irregularities which find expression in the pulse as intermissions and arythmia, while a high

tension may still be present by reason of the peripheral resistance. The subjective disturbances, such as difficult respiration, dyspnœa, palpitation, oppression of the chest after slight muscular exertion, even during an accelerated walk on the level, but especially on mounting stairs or an elevation, are vividly felt. Associated with them is a more rapid effusion of sweat than before, which covers the face and forehead of the patient in heavy drops; and after every great or prolonged muscular exertion, especially in summer or during nervous excitement, the patients are as it were bathed in sweat.

The secretion of urine diminishes; the irregularities astonish the patient: for some length of time he passes but little urine, then for several days in succession profuse quantities are evacuated. Later on the attacks of polyuria become progressively rarer and less marked. The cause lies partly in the increasing venous congestion due to the weakness of the heart, partly in the simultaneous affection of the kidneys by arteriosclerosis. If not before, now the high pressure from congestion or the disease of the kidneys causes the appearance in the urine of albumin, though not in large quantity. If the albuminuria is due to congestion alone, it soon disappears again when the heart action improves and the congestion lessens, whether spontaneously or in consequence of dietetic-mechanical or medicinal interference.

The pre-existing or perhaps now ensuing asthma assumes a grave aspect; the nightly attacks become longer and afflict the patient with intense pain, especially when further degenerative processes have affected the heart muscle, *i.e.*, when thrombotic patches and chronic myocarditis have ensued. The respiration during the attacks is more and more impeded and now and then assumes the true Cheyne-Stokes type. In addition there are precordial anxiety and stenocardic attacks which are extremely painful. These attacks may also have been present before, and been interpreted as nervous in character. At this time, however, the diagnosis becomes obscure; the pain in the heart which previously seemed purely nervous is assigned to another cause; and the attacks, though formerly painful and troublesome, have assumed a character dangerous to life. Intead of starting from irritation of the cardiac ganglia, which, as is well known, are of a sensory nature, the pain in the heart muscle is caused by embolism and thrombosis of the smaller or at first the smallest cardiac arteries and the irritation resulting from them. The gravity of the attack will vary according to the size of the occluded artery and the vascular region supplied by it, and according to the possibility of a more or less complete and rapid establishment of collateral circulation.

Stenocardia.—Either after some unusual exertion, especially after a full meal, strong mental emotion, or sexual excitement, or without such cause, when at rest or during sleep, the patients are suddenly attacked by a violent pain in the chest, usually in the region of the heart, which forces them to stop when walking, or to sit up or leave the bed at night. The pain may occupy various regions, either more to the left side near the heart or in the middle along the sternum or transversely across the chest toward both hypochondria. Especially characteristic is the radiation of the pain from the region of the heart into the left arm as far as the hand, which becomes weak and nerveless so that the patient finds it difficult and painful to grasp with it. The pain also radiates to the right side, but rarely as far down the right arm as the left, or it occurs at the same time more or less violently at the nucha near the occiput.

In severe cases, with occlusion of a larger artery, the pain may become so great that a sensation of faintness or true syncope occurs. The pulse is small, thin, frequent (130–140 beats per minute), irregular, or barely perceptible. The face is pale, the lips and cheeks are cyanotic, cold sweat covers the forehead, respiration is shallow, frequent (40–60 inspirations per minute), or irregularly intermittent. The patient avoids deep respirations because the changing intrathoracic pressure connected with them intensifies the cardiac pain. Not rarely the patients can breathe only while standing or somewhat inclined backward, half leaning, as the least raising of the diaphragm in another position materially increases the pain and thus impedes respiration. Percussion over the heart in such cases shows it to be enlarged in all directions, especially to the right, often beyond the right edge of the sternum, and on auscultation the heart sounds are indistinct, often barely audible, or associated with faint systolic murmurs due to a relative insufficiency resulting from the great distention of the cardiac wall. The attack may last a longer or shorter time, from a few hours to several days, according to the size of the injured vascular region and the destructive processes in the muscle. As the renal artery carries little blood to the kidneys, the pressure in the capillaries of the glomeruli has sunk very low, and the veins are overfilled with blood, the renal secretion is almost completely suppressed, and albumin is present in the scanty urine.

At the height of the attack or later on when a larger artery is occluded, especially the one running in the anterior longitudinal sulcus, death may occur either suddenly, or gradually by exhaustion of the heart, with symptoms of paralysis of the organ. This serious affection and such termination are not so frequent in arteriosclerosis complicating obesity as under other circumstances. Equally rare is

rupture of the heart from softening of the muscle, or after thrombosis of a larger vessel.

In most cases the attacks pass over after a shorter or longer time; the injury suffered by the heart muscle is repaired, a collateral circulation is established, and the muscular substance destroyed by the myomalacic process is replaced by a deposit of connective tissue. Should a larger portion of the cardiac muscle have perished and been replaced by connective tissue, the heart wall at that point becomes thinned more and more and finally an aneurism develops. This termination likewise is more rarely observed in cases of obesity and fatty heart.

After the stenocardic attack has passed the patient feels for a considerable time weak and wretched, but recovers gradually and the subjective condition is nearly as good as before. The attack may remain isolated or return after a longer interval, or slighter more frequently repeated attacks may increase in severity and one of them be fatal, or death may result from the sequelæ.

In the majority of cases, after recovery from the attack, the insufficiency of the heart increases, the arteriosclerosis has caused extensive muscular degeneration and chronic myocarditis, the dilatation becomes greater and is no longer compensated by hypertrophy. Fatigue of the heart occurs after a few contractions, and the muscle labors to propel the blood accumulated in the right heart and the lungs by incomplete, irregular, partly accelerated contractions, and to maintain the circulation approximately for the performance of the most important vital functions.

In the further course of the disease the congestions multiply, the excretion of urine becomes still more incomplete, the attacks of polyuria are rarer or absent, and on determining the differences between ingestion of fluids and excretion of urine large deficits are found which can no longer be compensated for by restricting the quantity of liquids consumed. No more surplus of urine is obtained, but a diminution of the fluids ingested is followed by a small excretion. The water consumed in the food and drink can no longer be completely expelled even by the greatest activity of the vicariously acting organs. The cutaneous arteries supply the sweat glands with less and less blood and while the patient perspires easily the secretion is not great enough to take the place of the lessened urinary secretion. The hydræmia increases, the water accumulates in the tissues, the return flow in the lymph vessels becomes more and more defective by reason of the reduced tension of the tissues resulting from the immense serous transudation and imbibition. The water accumulates first in accordance with the weight of the stagnant column of blood and the most restricted return

flow, *i.e.*, in the lower extremities, in the cellular tissue of the foot around the ankle, and forms œdemas which may disappear for some time after the circulation is relieved by spontaneous or artificial diuresis, but they soon return or increase rapidly from the start.

Wherever *œdema* develops the secretion of sweat diminishes more and more and finally ceases so that perspiration no longer appears even under the influence of great heat, in hot dry-air or in Russian and Turkish baths. Hence the greater the surface over which the œdema extends the more the excretion of water by the skin diminishes, and this in its turn adds to the hydræmia. The œdema spreads slowly over the lower extremities, above the thighs, and on the surface of the abdomen. The scrotum, penis, and prepuce, in women the labia majora and minora, swell and assume enormous and unshapely dimensions owing to the great transudation of serous fluid into the loose meshes of their cellular tissue, and this materially increases the troubles of the patients. The high pressure of the accumulated water and the saturation of the tissues as far as the epidermis may cause excessive stretching and tension of the skin, fissures, and detachment of the epidermis. The thin watery serum exudes from the wound, the epidermis is macerated, ulcers form, and erysipelas may appear and spread far over the legs and thighs, the scrotum, or the labia.

The condition of the patient becomes more and more deplorable. The congestion in the abdominal vessels, especially the portal system when the liver has undergone cirrhotic degeneration, leads to effusion of water into the abdominal cavity—ascites—with progressive reduction of space and crowding up of the diaphragm and further interference with respiration. Water also exudes from the vessels into the pleura and pericardium, causing hydrothorax and hydropericardium. The congested, nearly inelastic lungs, whose alveoli have already been much constricted by the ectasia of the capillaries resulting from the stasis of the blood, are compressed and their expansion during inspiration is more and more limited. On the other hand the transudation in the pericardium, aside from its effect on the lungs, exerts more or less pressure upon the surface of the heart and hinders its diastole and at the same time the passage of the blood from the overfilled rigid lungs into the heart. The respiratory and circulatory disturbances reach the highest degree. The patient can no longer lie down. He passes day and night sitting upright in bed or outside of it. The swollen, painful feet interfere with spontaneous movement. Suffering from continual dyspnœa he struggles laboriously for breath. Long-standing congestive catarrhs in the bronchi with the formation of abundant, tenacious, mucous or muco-purulent masses keep up the tormenting, painful cough and add to the dysp-

nœa. Owing to the weakness of the heart hemorrhagic infarctions and thromboses may form in larger or smaller pulmonary arteries. Blood in greater or lesser amount appears in the expectoration and renders it more difficult. Moreover, breathing is still more restricted by the shutting off of the region of the lung supplied by the thrombosed artery. The patient may die rapidly in consequence of the pneumonia and pulmonary œdema resulting from the injury, or if the infarcted region is small he may recover from it and continue his miserable existence.

If the patient is fortunate the last terrors of the disease may be preceded by a serous effusion into the brain—cerebral œdema. Sopor ensues and death follows before the patient regains consciousness. In other cases painful hours are still in store for him. The congestive catarrh involves additional bronchi in which the exudation grows more and more profuse while expectoration becomes more difficult, the dyspnœa has become extreme, the weakening heart can no longer overcome the weight of the blood, hypostatic pneumonias develop or the patient perishes without them from the slowly forming pulmonary œdema, after hours of stertorous breathing, pulseless, and covered with cold sweat.

The disease may terminate earlier by the alterations of the vascular walls due to the arteriosclerosis and atheroma, by their rupture through friability, by detachment of emboli and their deposition in some cerebral artery, by hemorrhage of the brain, and by embolism and thrombosis.

In obesity, especially the plethoric form, cerebral hyperæmia is a frequent symptom and finds particular expression also in the external appearance, in the flushed face, the distinctly pulsating carotids, the thick-set figure, the broad chest, the short neck, *i.e.*, the apoplectic habit. The patients complain of vertigo, headache, tinnitus aurium, muscæ volitantes, from which they are sometimes relieved by epistaxis. But even without the presence of true plethora, in hydræmia and serous plethora, the abnormally high vascular tension resulting from arterial sclerosis may lead to rupture of a vessel. It is generally caused by an increased pressure in the cerebral vessels, a psychical excitement, a hearty meal, sexual excitement, or great muscular exertion. Besides, an increase of venous pressure by straining at stool, by sneezing, screaming, or laughing may indirectly raise the arterial pressure and be followed by rupture of a vessel.

Prodromes may precede the attack and manifest themselves chiefly after hearty meals and in the presence of constipation by a marked feeling of heaviness and sluggishness, rush of blood to the head, flushing of the face even after slight physical and psychical excite-

ment, while the extremities feel cold and cause sensations of stiffness, numbness, and formication. Associated with them are the other symptoms of congestion, dizziness, tinnitus aurium, muscæ volitantes, general irritability, and restless sleep interrupted by alarming dreams, etc.

If an apoplectic attack has occurred the prognosis in general is always unfavorable. In most cases death ensues immediately or soon after the injury. When the location and size of the hemorrhage do not determine a fatal result and the patient recovers, fresh and more profuse hemorrhages soon follow and end in death. Only a small minority of the patients live for any length of time after the attack.

Glycosuria.—A grave complication of excessive accumulations of fat in the body is the excretion of sugar in the urine—lipogenous diabetes mellitus, glycosuria.

As regards the causes of this disease of the corpulent we are not yet fully informed. The capacity of the cells of the body for burning up sugar may be impaired by various causes, and of these different causes one perhaps is associated with a simultaneous protoplasm poisoning and pathological disintegration of albumin, while another is not. Numerous attempts at explanation are to be found in the literature. The inactive mode of life, the sedentary habit, the slight muscular labor may favor the accumulation of sugar in the blood as they do the deposition of fat. In the course of obesity the power of decomposition by the muscular elements is still more impaired by the facts that the fibrillæ of the muscles are crowded apart by fat, partly undergo fatty degeneration, and that the energy of their contractions is reduced by the slight restitution of the inogen resulting from the diminished supply of oxygen by the blood which is deficient in hæmoglobin, thus lessening the functional activity of the muscle in general. It is certain that the factors here enumerated may exert a restricting influence upon the decomposition of the carbohydrates; but we cannot consider them as the true cause of the diabetes, since they occur far more frequently and markedly in cases free from glycosuria. A better though still incomplete explanation of the etiology of diabetes in obesity has been furnished by the experimental investigations of Minkowski and von Mering who were able to produce an intense diabetes in dogs after extirpation of the pancreas. When the latter was only partially removed and the rest with its vessels left in the abdominal cavity, the diabetes failed to occur. When the remnant of the organ was subsequently extirpated the disease developed. But if only about one-tenth of the pancreas is left in the body a slight form of diabetes ensues in which the glycosuria is dependent solely upon the ingestion of carbohydrates.

In explaining the pancreatic form of diabetes Minkowski and von Mering assume that the pancreas supplies some substance, some ferment which is necessary for the destruction of glucose in the body, and Lépine expresses the view that the blood contains a glycolytic ferment serving for the destruction of sugar; that this is wholly or partly absent in animals after extirpation of the pancreas and in men affected with grave diabetes.

Formerly it was chiefly in the liver that the cause of diabetes was sought, although in extreme fatty degeneration of the liver after phosphorus poisoning and in cirrhosis of the organ no glycosuria develops. In order to decide this question Markusse subjected frogs to extirpation of the liver with the pancreas, and while glycosuria began in one or two days in frogs from which the pancreas alone was removed, no diabetes occurred when the liver also was removed.

The interpretation of this experiment is still a difficult one, and we are forced to assume either that a ferment is formed in the liver, which, without being sugar, is of importance for the development of diabetes; or else that the liver destroys some substance in the blood, which remains in the latter after removal of the organ, and itself destroys the sugar of the pancreatic form of diabetes. In many cases of obesity the disease of the pancreas has been studied by Balzer and others, besides the observers named, and the occurrence of fat necroses in the organ has been frequently determined. But the pancreas was as frequently found apparently normal on microscopical and macroscopical examination. Nevertheless the hypothesis may be maintained (von Noorden) that purely functional disturbances of the pancreas, which cannot be recognized anatomically, are sufficient to produce glycosuria. In connection with the etiological considerations it may be stated that it is improbable that the diabetes of obesity is of neurogenous origin, since corresponding affections of the medulla oblongata have thus far not been demonstrated.

The nutritive disturbance which is first and foremost in the diabetes of obesity is the early occurrence of disintegration of albumin, soon assuming considerable proportions, by which the amount of albumin, small as it is in the stage during which diabetes develops, is still further diminished. The increased disintegration of albumin in diabetes may be due to two causes:

1. The loss of nitrogen may be caused by defective nutrition, as the proteids of the food and the body albumin are no longer economized by the carbohydrates which are not burned up but changed into sugar. As the loss of calories derived from the carbohydrates must be replaced by transformation of albumin, and the calorie value of the albumin equals that of the carbohydrates, the great

losses of albumin suffered by the diabetic patient are explained. When obesity is present the fat is likewise drawn upon for combustion, perhaps at an earlier period, and the patient will lose fat as well as albumin and become thinner.

2. Loss of nitrogen may also result from a toxic disintegration of albumin, and while the decomposition just mentioned may be called physiological, this destruction of albumin must be considered as pathological and classed with that occurring in fevers, phosphorus poisoning, leukæmia, etc. Such a disintegration of albumin v. Mering claims to have demonstrated, since the diabetic patient observed by him, after deducting the amount of albumin transformed into sugar and passed in the urine, was still losing nitrogen in the stage in which a considerable quantity of beta-oxybutyric acid is excreted in the urine. Further confirmatory clinical observations are yet to be furnished.

Of importance in this connection might also be the fact demonstrated by Külz, that some carbohydrates (levulose, inulin, cane sugar, milk sugar, etc.) are destroyed in the body of the diabetic patient, while others (grape sugar, starch, etc.) are not.

The sugar in the urine of the diabetic is grape sugar (glucose, dextrose); in a few rare cases only do we also find levorotatory sugars.

Besides, the power of destroying sugar is never completely lost, and even in the gravest cases thus far examined the quantity of sugar in the urine, though carbohydrates were supplied in abundance, was less than the amount of carbohydrates present in the circulation. According to Külz, the decomposition seems to be effected more largely in proportion as the ingestion of carbohydrates within a brief period is greater, and the losses by sugar formation augment the more the carbohydrates are distributed throughout the day. Additions of fat to the diet in diabetes can never increase the glycosuria, so that the loss of sugar by the patient can be reduced to the minimum by foods containing a moderate amount of albumin and a plentiful supply of fat. In like manner the combustion of sugar is as a rule augmented by muscular labor and thus the glycosuria diminishes while the nutrition remains the same. In the same way as an ample supply of carbohydrates leads to their increased decomposition and thus economizes albumin, so does the augmented physiological consumption of sugar by muscular labor, at least in the majority of cases.

Glycosuria may be combined with obesity in such a way that the patient's organism has lost only some of its power to burn up sugar, while the synthesis of the carbohydrates into fat is still effected. Under such circumstances, with the plentiful nutrition to which these patients are particularly inclined, obesity is sure to develop. Such

patients are diabetic, but they do not always excrete the sugar by way of the urine, or do so only in a minor degree, the carbohydrates being transformed into fat and the obesity masks the diabetes—diabetogenous obesity. But in most cases of diabetes associated with corpulence, lipogenous diabetes, not only is the combustion of carbohydrates greatly restricted, but also their transformation into fat, which in ordinary cases of diabetes is nearly as much impaired, has suffered some diminution.

Glycosuria may occur spontaneously or may be hereditary like obesity. A special predisposition to either of these diseases seems to be also peculiar to some nations and races, *e.g.*, the Jews.

Seegen first called attention to the frequent occurrence of diabetes mellitus in obesity. Among his 140 cases were 52 in which the glycosuria was preceded by obesity. Pfeiffer places the percentage of obesity as high as 33, while Kisch states that in cases of extensive hereditary obesity more than half become affected with diabetes mellitus, as opposed to about fifteen per cent. in the acquired forms. In cases of hereditary tendency the diabetes may occur without obesity or supervene after the development of the latter, while other cases become phthisical, or, after the patients have in earlier life presented symptoms of beginning phthisis, they become later on rapidly and extremely obese and finally succumb to diabetes.

The age at which diabetes develops is between thirty and forty years, though the disease is also frequent beyond the fortieth year.

The first symptoms by which the development of diabetes is manifested are apparently favorable to the patient, since he gradually becomes thinner, his inconveniences diminish without loss of appetite, while the thirst and the excretion of urine increase noticeably. The emaciation progresses steadily, independently of anything done by the patient. The ingestion of food is still plentiful and the muscular activity the same as that under which the corpulence developed. Therefore, when a corpulent person loses weight steadily though slowly, and this fact is not explained by a change in the diet directed toward the reduction of the obesity or by increased muscular labor, the indication is urgent to examine the urine, in which sugar in greater or less amount can nearly always be demonstrated. The appetite then gradually lessens, the nutrition suffers, losses of albumin and fat ensue, thirst increases, more and more fluids are consumed, chiefly water, and large quantities of clear, light-colored urine of high specific gravity are passed. The diabetes has become fully developed and can no longer be mistaken.

The course and termination of the disease vary greatly. When the presence of sugar in the urine is chiefly due to the excessive in-

gestion of carbohydrates (the milder form) the glycosuria may disappear if a strict antidiabetic diet is maintained. Thus I had under treatment a female corpulent patient in whom glycosuria occurred every February, when she consumed large quantities of honey, persisted several months, and again disappeared in July or August under strict diet. Cantani ascribes the frequent occurrence of diabetes in Italy to the preference of the inhabitants for farinaceous and sweet dishes. In other cases the diabetes induced by unsuitable nutrition persists for a longer time, increases in intensity, and while it finally improves more or less under strict dietetic treatment it never disappears completely.

Hereditary diabetes is less influenced by treatment and runs a more rapid and serious course.

The termination of the diabetes of the corpulent is the same as that of the form occurring under other circumstances: simple marasmus, pulmonary phthisis, general furunculosis and the formation of carbuncles, nephritis, more rarely diabetic coma. The ordinary termination of obesity by cerebral hemorrhage, paralysis of the heart, and dropsy may also end the disease.

Cancer.—Lastly mention must be made of a complication observed in obesity which is frequently recorded in the older literature, namely, carcinosis.

The symptoms, course, and termination depend upon the importance of the organ attacked by the carcinomatous process, upon the variety of the malignant new formation, and the prevailing resistant power of the organism by which the occurrence of cachexia is kept in abeyance for a longer or shorter time.

Diagnosis.

The diagnosis of obesity in general is not a subject of any great difficulty. The form of the body and the habitus of the patient allow of no doubt concerning the kind of nutrition disturbance in question. The matter is different when we have to distinguish more exactly just what form presents itself before us and in what stage it is, how the heart-power and disturbances of circulation are to be taken into consideration, how the single symptoms are to be explained, by what complications the disease is influenced, and in what degree.

The *plethoric* and *anæmic* forms are easily recognized in most cases, when the general state of nutrition of the patient, the putting on of fat, formation of blood, complexion, color of the skin, paleness and cyanosis of the mucous membranes, as well as the other

symptoms fully described under symptomatology are examined in a more careful manner. Even the *hydræmic* form developing finally from these other forms will be usually distinguished very easily from the two others upon the same grounds, and especially when the duration of the existing disturbances of nutrition is considered. But there are many cases where it is not possible to determine the quality of the blood from the existing symptoms, and a direct examination of the blood, taken into account with the existing disturbances of circulation, can alone lead to a positive diagnosis. At the same time it is to be remembered that in most cases we receive for investigation only venous blood, and therefore we must judge of the quality of the patient's blood with great care, and only after investigating the amount of hæmoglobin contained, the specific gravity of the whole blood, and especially of the serum, perhaps also by counting the blood corpuscles, but never from an estimation of the hæmoglobin or blood corpuscles alone. According to the degree of disturbance of the circulation we have to deal with an accumulation of the solids in the venous blood—stasis and concentration, as I have designated this manifestation. The amount of hæmoglobin, as well as the specific gravity of the whole blood with especial reference to the number of blood corpuscles, may be considerably increased and notwithstanding this hydræmia may be present, the specific gravity of the serum being very low and the blood containing much water. The faulty conclusions drawn from the examinations of blood made by Lichtheim, Bamberger, and others, have their origin in the fact that there have been conditions overlooked by them. A too large percentage of hæmoglobin is always suspicious, although the patient's other symptoms permit of no conclusions as to the advanced disturbances of circulation. By testing the specific gravity of the serum in such cases we find it to be below the normal standard, and we have nothing else to deal with than a blood rich in albumin and hæmoglobin. On the other hand, the specific gravity of the serum alone or even together with the blood corpuscles would not indicate at all the amount of hæmoglobin, and though the latter may seem to be normal, anæmia and chlorosis can be present. In all forms of obesity experimental researches are to be made as to the fluids taken in and the secretion of urine, both while the patient takes his usual allowance of liquids and when the latter are greatly diminished.

Important for prognosis and therapeutics is the early recognition of the *arteriosclerosis* that often develops even in the earliest stages of obesity. Although we may not be able to observe changes in the vascular apparatus, yet resistances are created by the very beginning

of the sclerotic process, resulting in decided tension of the pulse. A rise of blood pressure to 150 mm. of quicksilver or over may be regarded as a sign of sclerotic process, even if latent. In the further course of the affection the artery becomes tortuous under the high blood pressure, although a rigidity of the walls may not yet be appreciable to the touch. Where the artery is superficially situated, such as is the temporal, or more rarely the radial, the fact of its being more or less sinuous, especially under conditions of excitement, is clearly apparent or can be made visible by cautious friction with the hand or a piece of cloth, etc., thereby irritating the dilators and causing enlargement of the vessel's lumen. In advanced cases a failure to recognize the rigidity of the vessels is no longer possible if careful palpation is made.

Attacks of stenocardia and cardiac pain are peculiar to sclerosis, and differ essentially from a neurosis by reason of occlusion of the vessel from embolism and thrombosis of the coronary arteries and of consequent myocarditis, myomalacia, formation of callosities, aneurisms of the heart, and heart rupture. The attack is only distinguished by considering together all the symptoms which go to make an existing sclerosis of the artery probable, more particularly the intensity of the heart pain, the characteristic radiation toward the left arm, the great sense of prostration, and swooning attacks which may even go on to actual fainting fits, and especially the coincident existence of dyspnœa. In cases of functional trouble, the stenocardia may be of extraordinary severity and may even be accompanied by the characteristic radiation of pain toward the left arm; but in these cases we always miss the severe dyspnœa which is never absent where there is arteriosclerosis, and which is, therefore, a valuable diagnostic criterion.

The frequent association of arteriosclerosis with obesity, especially at about forty years of age and upward, and the fatal consequences which result directly from overlooking the same, make it our duty to consider as carefully as possible in each case of obesity in its later stages the existence of an arterial change.

When *atheroma* of the vessels has been produced, the degeneration of the vessel's walls may be immediately recognized by examination of those arteries which are superficially situated and accessible to investigation. On the other hand, in cases of simple sclerosis we must always think of the possibility that one or another of the vessels existing in the interior of the body may have undergone atheromatous degeneration and may produce by rupture a dangerous hemorrhage, especially in the brain.

Just as easily perceptible are the *gout* and the *uric-acid diathesis*

frequently connected with obesity and atheroma. Disease of the joints, the presence of gouty pains, and the investigation of the urine soon leave no doubt as to the existing complication.

The condition of the kidneys, *congestion-albuminuria*, *contracted kidney*, and genuine *parenchymatous nephritis* (Bright's disease) will be shown by the chemical analysis of the urine and the microscopic examination of the sediment. Occasional slight attacks of albuminuria and the appearance of hyaline casts in the urine always prove existing congestion.

The early recognition of *diabetes mellitus* has the greatest influence upon the patient's future. When without physiological or therapeutical reason we observe our obese patient spontaneously and rapidly losing weight and becoming emaciated, it is of the utmost importance that we test the urine, even if no marked thirst is complained of and the amount of urinary secretion has not been greatly increased. In these cases we shall almost invariably find a more or less advanced condition of glycosuria.

If *œdema* has set in during the last stages it is not very difficult to distinguish the tensely stretched masses of fat of ordinary adipose tissue from the doughy swelling of œdema which so characteristically retains the mark of finger pressure for a long time.

Furthermore if *emphysema* of the skin has developed as is sometimes the case, it will scarcely be possible to mistake the swelling caused by air in the tissues, which gives a crackling under pressure, for deposits of fatty matter or for œdema.

Prognosis.

Varying according to the causes, form, symptoms, and complications, the prognosis of obesity cannot be always uniform, but will present itself in all transition stages from one which is relatively or even positively favorable, up to one which is decidedly bad.

According to the fundamental causes, the prognosis depends in the first place upon the hereditary disposition, or upon the disturbances of nutrition acquired by an unsuitable manner of living; in case of the latter it will be much more favorable than in the case of the former. The prognosis also varies with the form of obesity, and in case of true plethora is comparatively better than in the anæmic form. Of decided importance here is the individuality, since the essential results depend upon the patient's obedience and upon his subordination to dietary rules and upon his subsequently following out a suitable mode of life. The prognosis is most favorable in cases of the inherited form of obesity which comes on in the first

years of life, where it is not very difficult to bring the children into a normal state of nutrition by proper regulation of the diet.

If on account of heart-insufficiency there exist any more or less extensive disturbances of the circulation, or if hydræmia or accumulation of water in the blood and tissues is already present, the experimental comparison of the amount of fluids regularly taken and of the quantity of urine regularly secreted within the twenty-four hours will supply the most reliable indications.

For this purpose the patient should take during two days, for instance from 8 A.M. of one day to 8 P.M. of the following day, as much fluid as he is accustomed to, but this as well as the secretion of urine is to be measured and the amount written down together with a statement of the time within which both obervations have been made. After this for the next two days the fluids taken ought to be reduced to 700–1,000 c.c., according to the size of the patient, especially with regard to the condition of his vascular apparatus, and the same notes are to be again made. If now with the reduced amount of fluids taken, a plus quantity of the urinary secretion, especially if a considerable increase of the same is produced, we can always draw the conclusion that the heart-power is not as yet too much weakened, and that the function of the kidneys is not much disturbed, therefore the prognosis will be the more favorable. That will be all the more the case, if not only a relatively, but even an absolutely greater quantity of urine is excreted than when the patient was taking a disproportionally larger quantity of fluids.

But if by reducing the fluids not only no increase takes place but a very considerable minus quantity is noted, we may always consider this result of the experimental observation of unfavorable prognosis as to the course of the affection. On the other hand, if the quantity of the urinary secretion is but a little under that of the fluids taken, it is to be considered as an increase compared with the normal secretion, because normally about 18 to 20 per cent. of the water of the fluids, taken as such, as well as the water contained in the solid food, is used up in respiration and perspiration, and a reduction of these percentages is to be considered an increase of the urinary secretion.

Of prognostic importance is also the condition of the circulatory apparatus during such physical exercise and muscular work as are required in walking and climbing. The prognosis becomes unfavorable when the heart muscle no longer reacts to motor impulses produced by physical exertions, when the pulse instead of becoming more frequent and stronger becomes threadlike and overfrequent or irregular, and when, instead of a strong or at least plainly perceptible palpita-

tion, there is only dyspnœa, excitement, oppression, and labored breathing.

When a patient subject to obesity is attacked by intercurrent febrile diseases, the prognosis of the latter is unfavorable as compared with febrile diseases of equal gravity in other persons, for the reasons above mentioned. Furthermore, convalescence and recovery are very apt to be slow and incomplete, because of weakened regenerative power and slow formation of red blood corpuscles.

Arteriosclerosis, especially of the coronary arteries of the heart, makes the prognosis much more unfavorable. In such cases we should be guarded in making a prognosis, even in mild attacks of stenocardia which are in themselves insignificant, because we can only draw the conclusion from these attacks that the blood-vessels of the heart are affected, but we cannot say to what extent they have suffered; furthermore these milder attacks are often followed by more severe and even dangerous ones, and possibly by intracranial hemorrhage.

In cases of sclerosis the treatment is rendered more difficult in that the mechanical part cannot be carried out to the extent which the indications would require were it not for this existing complication. These severe attacks have an unfavorable influence upon the prognosis in proportion to their severity and duration, since each attack works structural changes in the heart muscle, increasing its insufficiency and hastening death. The milder attacks may be of importance as regards treatment and the course of the disease in so far as they direct our attention at once to the existence of dangerous conditions connected with the heart vessels which threaten the patient and permit us in time to take precautionary measures against them.

Diabetes aggravates this disease in proportion to the quantity of sugar in the urine and the decomposition of albumin. The prognosis is rendered less unfavorable if the appearance of sugar in the urine is exclusively or for the greater part due to the ingestion of sugar-forming substances, and if it decreases materially or disappears entirely when the latter are reduced or when an absolutely diabetic regimen is carried out.

These patients may be made comfortable for a long time if we always carefully watch the extent of the glycosuria which stands in direct proportion to the decomposition of albumin. It is also to be remembered that these milder cases in the majority of instances become transformed into severer ones. In case the quantity of nitrogenous substances in the urine surpasses the equivalent of the undecomposed sugar the prognosis is altogether unfavorable and occurrence of diabetic coma is at any moment to be dreaded.

Albuminuria, when appearing as congestive albuminuria accompanied by slight congestive œdema and without any complication, may disappear, if the heart muscle can be strengthened, and if the patient is not too old.

After the occurrence of chronic nephritis, contracted kidney, and general dropsy, the organs never again regain their former condition for any length of time, and for the most part death after a short period ends the long and varied course of the disease.

Treatment.

Prophylaxis.

All persons do not have the same tendency to grow stout, and a certain proportion of mankind seems to possess a peculiar immunity to fat production, and to remain lean in spite of consuming with the nourishment a surplus of fat-producing substances. Furthermore it is impossible to foretell whether a given person will become excessively fat or not, and the formation of fat is a physiological process which ought to be limited to a certain extent but in nowise should be suppressed in anticipation of what may happen.

It follows that the prophylaxis against a possible adiposity and the tendency to it affects two principal categories of individuals, first those in whom there is an hereditary tendency to the disease (and this not only applies to the adult but also to children and infants at the breast), and secondly individuals who have already suffered from obesity and who through some therapeutical measures have lost their surplus fat and become relatively lean.

Prophylaxis in Early Life.

As to the first category we have to do principally with an hereditary disposition. The children of such parents, according to the literature, already at birth show a high degree of adiposity, or they may take on abnormally large quantities of fatty tissue a few months after birth. When such cases come under treatment the physician has first to ascertain if the character of this adiposity, hereditary in that special family, is of the plethoric or of the anæmic form, and in what manner this hereditary character manifests itself in the individual in question.

a. If the hereditary obesity shows itself in the family in the plethoric form and if a young or older child shows the unmistakable signs of this form, the dietetic treatment will consist principally in a diminution of the fat-forming substances in the dietary. The principles

of treatment of obesity as formulated further on will here as well hold good, taking into consideration the age and individual conditions.

Children and nursing infants who are well nourished and full-blooded, and whose progenitors suffer from the plethoric form of obesity, have to be raised on as rational a plan as possible, either on the mother's milk or artificial food.

If the mother suffers from obesity and at the same time is able to nourish the child, it is not advisable to permit her to do so, if it can be avoided, but it is better to allow the child to be brought up by a suitable wet-nurse in whose family no hereditary predisposition to this affection is present. If the child is, however, nursed by the mother, the diet of the latter must be so regulated as to exclude all superfluous fat-producing substances (especially beer in those countries where it is the customary beverage). The nurse's diet must also be similarly regulated, though strict directions are not required. If the child is raised artificially cow's milk is best used prepared with Soxhlet's sterilizing apparatus. Farinaceous substances and other infant foods of whatever name are to be altogether excluded so long as the child's fat-production does not sink below the norm.

After the first years are passed we must choose from among the various articles of food, according to their proportion of albumin and fat, those which are favorable to the retardation of fat-production. In cases where there is but little adiposity present the carbohydrates, butter, and articles prepared with fat are admissible. Where there is a preponderance they have on the contrary to be diminished as much as possible, and at the same time the child's growth, blood production, digestion, powers of assimilation, the action of its heart, and the functional power of its muscular apparatus must be kept in sight and taken into consideration. In the later years, especially in youth and adolescence, on entering upon the age of puberty, the conditions relating to the development of sexual activity, as they affect the growth of the bodily tissues, are the indications according to which the individual has to be nourished. If there is little tendency toward obesity in these years, the supply of fat-forming substances must not be too much reduced. Furthermore it is important not to lose sight of the fact that the amount of albumin of the body depends upon the quantity of the fat, and that if the latter suffers too great a reduction, the body cannot preserve its required proportion of albumin, and the formation of blood will therefore soon sink below the normal. The muscular development will be retarded or diminished, so that the individual finds himself weak, powerless, and unable to work. The laws of nutrition must always be fresh in the physician's mind. The exertion of the muscular apparatus caused by activity and all kinds

of gymnastics which heighten the nourishment of the muscles and retard the accumulation of fat, are especially to be considered in boys and youths; but even in girls this must not be neglected, nor put too much into the background whenever the education calls forth mental activity or where studies or more sedentary occupations prevail.

b. If the signs of anæmia are noticeable in infants at the breast or in older children in the first years of life, along with a pronounced obesity, preparations of iron are early indicated and should be given, according to the age of the child, in addition to a dietary which aims at regulating the amount of albumin and fat. In later years the activity of the muscles is to be stimulated in proportion to the existing functional power of the muscular apparatus. Mineral baths containing iron and salt baths should be prescribed to meet the indications furnished by the presence of scrofula. Sojourn in the fresh, pure air of the woods, mountains, or at the seashore, cold ablutions and cold frictions once or twice a day are advisable. Cool baths stimulate powerfully the circulation and increase the powers of resistance of the surface of the body against external injuries.

The influence of these measures upon resolution of the fat, and upon what is commonly called metabolism, must not, however, be too largely depended upon.

Prophylaxis in More Advanced Life, and After Effective Reduction of the Fat Under Treatment.

In this section we shall consider the prescriptions suitable for a patient whose surplus fat has been reduced to the norm by therapeutic measures, which will depend entirely upon previous changes in the organs which resulted in the accumulation of fat, and upon the condition of the organs after the consumption of the superfluous fat, especially taking into consideration the existing condition of the heart, the circulation, the blood, the amount of albumin, the activity of digestion, and the functional power of the muscular apparatus.

Prophylaxis, therefore, has mainly to be adapted to the individual case and has to be in harmony with the therapeutic measures, especially in reference to the dietetic-mechanical treatment under which fat reduction has taken place. We shall return to the subject of prophylactic treatment after successful reduction, in a subsequent paragraph.

The prophylaxis against adiposity in later years in adults whose condition of health is otherwise normal but who have an hereditary taint consists more in general dietetic measures, regulation of diet, promotion of muscular activity in order to quickly burn up superflu-

ous fat-forming substances which have been introduced to the economy. The diet of such persons has to be regulated in the following manner: 1. So that the quantity of albumin is not imperfectly burned up in case the diet is maintained for a long time, *i.e.*, for years. In the latter case uric acid would accumulate in the blood, especially if there should be present an hereditary disposition to the uric-acid diathesis and to gout. In the same way a too exclusive meat diet may produce dyspeptic symptoms, catarrh of the stomach, and digestive disturbances. 2. The supply of fat and carbohydrates ought not to be diminished so that the fat which is normally present is attacked and the albumin of the body is thus endangered. The quantity and quality of food and liquids must be the same for patients as mentioned above, that is, must be the same as for those who have lost their superfluous fat by dietetic and mechanical treatment (see below). In regard to bodily exercise the same rules must be followed, and visits to health resorts and a prolonged stay in mountainous regions should be encouraged. Alpine excursions must be prohibited at first and ascensions of mountain peaks must be allowed only when the heart action is normal. Gymnastics, horseback riding, bicycling, rowing, swimming, if not carried out in too sportsmanlike a manner or to extremes, will increase the strength, the formation of body albumin and of blood, while the formation of fat will be limited by these measures.

Treatment of the Abnormally Increased Formation and Storing up of Fat in the Body.

A. Dietetic Treatment.

In Relation to the Proportion of Body Fat.—In relation to the proportion of fat in the body we have to distinguish the following classes of cases and the indications concerning them according to the before-mentioned rules.

a. In cases where there is an abnormally increased quantity of fat in plethoric patients with unimpaired or only beginning changes in the heart action, the diet prescribed aims at (1) increased supply of albumin; (2) decrease in the fat-producing substance; and (3) little or no diminution in the supply of liquids below the physiological amount (1,500 c.c.).

b. Cases of adiposity in anæmic patients, viz., serous plethora. These require (1) an increase of the quantity of albumin, and simultaneously (2) a diminution of the fat-forming substances and eventually of the liquids taken.

c. Cases of adiposity in adults with hydræmic symptoms, in

whom not only the amount of albumin but also the abnormally increased amount of fat is slowly wasting away. The nourishment of such patients requires, (1) together with the increase of albumin taken, a sufficient allowance of fat and carbohydrates, or even an increase in the same, in order to prevent a sudden falling off of fat, and (2) a diminution of the liquids taken. The dietetic rules as laid down by me for the treatment of general adiposity are based in the first place upon pathological changes in the heart and the amount of circulatory disturbance caused by the latter. In this way they differ materially from the dietetic rules formulated by previous authors. In order not to overburden the action of the heart and the circulation it is necessary to consider not alone the quality but above all the quantity of solids and fluids taken. If the circulatory function is disturbed only a slightly excessive quantity of both liquids and solids, or of water alone, will do harm. The usual consequences, then, are a feeling of oppression, palpitation, dyspnœic excitement of a sudden and distressing nature, and difficulty of breathing. After a too hearty meal or too free consumption of liquids death may ensue in pronounced cases even after slight exercise or bodily exertion through paralysis of the heart. It follows that the temporary amount of fulness of the digestive apparatus, its displacement on the side of the thorax, and the overburdening of the blood by the food and liquids absorbed must determine the apportionment of the several meals. Only when these factors are kept in view, factors which bear upon the insufficiency of the heart and changes in the circulation, can a diet based on increased oxidation of the body fat be thought of. In patients whose circulatory apparatus is relatively sound, that form of obesity which is purely of a plethoric character, the change in the quantity and quality of food as laid down in the rules governing the nourishment (see etiology), together with a change in the patient's manner of life, *i.e.*, a change from too much rest and ease to muscular exercise and activity, are sufficient to produce an extensive reduction of the stored-up fat by oxidation, and at the same time to prevent an additional new formation of the same out of those articles of food which are least liable to be transformed into fat.

The most eloquent advocate of a diet consisting almost wholly of nitrogenous substances was Louis Banting, who published an account of Harvey's method according to which the diet was as follows:

(1) In the morning: 120–150 grams of meat or fish, with the exception of pork and salmon, tea without milk and sugar; 30 grams of toasted white bread.

(2) For lunch: 150–180 grams meat, vegetables exclusive of potatoes, 30 grams toasted white bread; two to three glasses of red wine

or sherry. No farinaceous dishes, no champagne, port wine, nor beer.

(3) Afternoon: 60–100 grams of fruit; a little toast, tea.

(4) In the evening: 100–120 grams meat or fish; one to two glasses of red wine, claret.

The use of water is permitted without limit.

Albumin.—This diet as laid down by Harvey is characterized by its high percentage of nitrogenous food, so that the masses of fat stored up in the body must be surely attacked in the physiological processes, and a quite considerable reduction of fat can be secured.

However it happened very soon after this publication of Banting that there were a number of individuals who when they followed out this diet for a considerable period decreased in weight, but finally became so weakened and miserable, nervous, and sleepless that the treatment had to be interrupted. In others the continued meat diet caused dyspeptic symptoms with consecutive catarrh of the stomach and intestinal tract.

The cause of these manifestations was on the one hand the impossibility of the human body to maintain its metabolic equilibrium during the process of feeding with exclusively nitrogenous substances. No fat and carbohydrates being taken in, the quantity of albumin was soon endangered, being liable to be partly used up in the production of the requisite calorie values necessary to the maintenance of life. Furthermore the food, which was in itself already insufficient in quantity to maintain proper metabolism of the nitrogenous substances, could not be properly digested, and gave rise to diseases of the stomach and intestines. It follows that we have to dispense with a purely albuminous diet on account of its slight value as a heat-producer. Indeed such a diet, in a quantity which to be sufficient would have to be very large, would usually not be digested and assimilated; but if together with the albumin so much fat and carbohydrates are taken in as to maintain nitrogenous metabolism, and if by greater muscular activity more non-nitrogenous substances are decomposed in proportion than fats and carbohydrates are introduced with the food, the deficiency of these latter substances will be made good by consumption of the fat deposited in the body, *i.e.*, the obesity of the patient will be diminished and he will become leaner. If this process of fat oxidation due to muscular activity is repeated at short intervals, while at the same time but small quantities of fat and carbohydrates are given with the food, the fat stored up in the body grows less and less until it finally attains a figure below which we do not want to go. The supply of nitrogenous food must, aside from its influence upon fat oxidation, be larger, because in

the majority of cases the patients are already anæmic and most of the muscles of locomotion and of the heart have become weak and atrophic. The new formation of muscular fibres and the increase in volume of those already present, which would result from an increase in the metabolism caused by muscular activity, require an augmented supply of albumin.

Fat and Carbohydrates.—In the exhibition of fat-forming articles of food we must discriminate between

a. Those cases in which the respiratory and circulatory apparatus have not been markedly disturbed, and where the activity of the muscular apparatus and a considerable amount of bodily exertion is still possible.

b. Those cases in which the blood is of anæmic or hydræmic quality, and advanced venous stasis reduces the absorption of oxygen in the lungs to a minimum, and where slight muscular exertion exhausts the oxygen, interferes with respiration, and causes dyspnœic symptoms.

In the first category, where the energy of cellular activity is as yet unimpaired, a liberal consumption of fat and carbohydrates can be allowed, since through the increased muscular activity and bodily exercise the metabolism is likewise increased. In the latter cases the use of fat and carbohydrates must be reduced to smaller proportions, and by simultaneous reduction of the body fluid by decrease in the fluid supply the circulation is rendered freer, and the liability of exciting dyspnœic conditions is abolished.

Fat and carbohydrates and albumin differ in relation to fat-formation in the body, in this way, that the proportions of these food stuffs are equivalent or isodynamic which produce the same quantity of heat during the process of oxidation into carbonic acid. Consequently 100 grams of fat replace 211 grams of albumin, 232 grams of starch, 234 grams of cane sugar, 256 grams of grape sugar, or a mean average of 240 grams of carbohydrates. Since one part of fat represents an isodynamic mean average of 2.4 parts of substances comprised under the term carbohydrates, we can always supply the body with more than twice the quantity of these substances until an amount equivalent to one part of fat is reached. The possibility of exceeding the limits prescribed by the diet is consequently less when carbohydrates instead of fats are given.

The body stores up fat if more than 118 grams of albumin and 259 grams of fat, a total of 377 grams (2,894 calories) are taken in. On the other hand 110 grams of albumin and 600 grams of starch, a total of 710 (2,944 calories) may be given without producing a deposit of fat. With mixed diet the limit lies near 118 grams of albu-

min, 100 grams of fat, and 368 grams of starch, a total of 586 grams (2,923 calories). Consequently we have a rather large choice in the selection of a diet, as well in quantity as in the quality of fat-forming substances. If we want to bring about decomposition of the fat already accumulated in the body, we do so best by diminishing the supply of fat and by permitting a certain quantity of carbohydrates.

If we take into consideration the different forms of obesity and their various stages, viz., those different conditions of nutrition, plethora, anæmia, and hydræmia, the amount of heart insufficiency and of circulatory disturbances, the general state of the constitution and what is left of the working power of the muscular apparatus, the kind of nourishment or fattening material, the ability to digest and absorb, the adaptation of the digestive system to a certain diet, and the numerous complications, it will become clear that it is impossible to formulate a *régime* or diet which holds good for all cases and at all times. We have to consider every case by itself and regulate the dietetic-mechanical treatment according to the results of examination and observation during the course of treatment.

The diet to be ordered in the treatment of obesity will therefore not be according to a general formula or a pattern, as it were, holding good for every case, but our efforts will consist only in fixing the limits as regards the supply of albuminous and fat-forming substances, and as regards the quantity of the one or the other to be allowed in a given case according to the general indications above set forth, and according to the special indications in each individual case.

In the first edition of my work upon the therapeutics of circulatory disturbances, where I took occasion to discuss fat reduction in patients whose circulatory apparatus was disturbed, I have already considered these points and formulated two diet tables. The latter are not to be considered as two sets of cast-iron rules or patterns, but indicate merely the limits within which the prescription of diet must move to adapt itself to each case, whether moderate in intensity or extreme.

This diet, which has given me good results in all cases during the past twenty years, and which, consequently, I have no reason for giving up, fixes the quantity of albumin, fat, and carbohydrates at the following figures, which I have found by calculating the diet in a very large number of observations:

	Albumin	Fat	Carbohydrates	Calories.
Minimum:	156	25	75	1180
Maximum:	170	45	120	1608

Since the number of calories may rise during exercise from 2,500 to 3,500 and over, the difference of 1,320 and 892 or of 2,320 and 1,892 must be met by the burning up of the fat of the body.

Supply of Liquids.—Not only the decrease of weight but also the reduction of the patient's fat depends materially upon the reduction of liquids in the body, the increased excretion of water, and the decrease in the supply of liquids in food and drink.

We have already discussed above (see Etiology) the influence of a diminished supply of water. Wherever there is a lowered heart action and circulatory disturbances exist, the success of treatment goes hand in hand with a diminution of the supply of liquids, according to the individual case, because by freely supplying the body with liquids, especially in the form of drinks, the heart action is at once considerably increased during a period of muscular activity.

The insufficiency of the heart muscle, the starting-point of most of the dangers of adiposity, is very considerably diminished by lowering the supply of liquids.

The production of forcible contractions of the heart is only possible where the resistance in the circulation is abolished as far as possible, where there is no overdistention of the vessels by increased fluid supply, where the circulation is not overburdened, and finally if the heart is able to force along the rush of blood.

An overburdening of the circulation can be produced by a relatively small supply of fluid which will augment the disturbances of circulation already existing, the stasis and peripheral resistance. The supply of liquids furnished as drinks, therefore, must adapt itself to the condition of the circulatory apparatus. Where the action of the heart is normal it ought not to exceed the physiological measure of 1,500 c.c. and only in cases of very tall patients and high daily temperature may it be increased to 1,800 or 2,000. In other cases the measure must be lower and reduced to from 750 to 1,200 c.c. More points, especially in regard to the amount of secretion by the kidneys, will be given below. The water introduced in the solids is excreted entirely through the skin. In the following tables I will give some points of value in the regulation of different diets. It will be easy to fix the diet in any given case according to its necessary supply of albumin and according to the quantity of fat-forming substances —fat and carbohydrates—which may be allowed. Thus the table permits us to individualize in the most minute way.

In this diet list it is evident that the fat may be replaced by carbohydrates in a quantity adapted to the special case or the carbohydrates may be replaced by fat. In this substitution we must be guided by the individual peculiarity, the facility with which the pa-

TABLE I.—*Special Diet List in Circulatory Disturbances.*

Liquids taken	Quantity in Grams or Centigrams.	Water contained.	Albumin.	Fat.	Carbohydrates in grams.	Analysis after
			Caffein.			
Morning (7–8 o'clock).						
Coffee	120.0	113.6	0.21	0.62	1.7	König.
Milk	30.0	26.2	1.29	0.96	1.2	König.
Morning (10–11 o'clock).						
Port wine	50.0	38.7	0.8	....	3.0	König.
(Or Pfälzer wine	100.	86.1	....	....	2.4)	König.
(Or clear soup [bouillon]	100.	99.1	....	0.8	....)	
Noon (1 o'clock).						Reuk.
Wine (Pfälzer) / Water	200.	172.2	....	....	4.8	König.
Afternoon (4 o'clock).						
Coffee	80.0	75.6	0.12	0.4	1.1	König.
Milk	20.0	17.5	0.7	0.7	0.9	König.
Evening (after 7 o'clock).						
Wine (Pfälzer)	200.0	172.2	...	....	4.8	König.
(Or water	250.0	215.3	....	....	7.2)	König.
Total	750.0	616.0	3.12	2.68	17.5	

Food taken.	Quantity in grams.	Water contained.	Albumin.	Fat.	Carbohydrates in grams.	Analysis after
Morning.						
Fine wheat bread	25.0	8.9	1.8	0.1	14.6	König.
Two soft boiled eggs	90.0	66.2	11.2	10.8	0.4	König.
(Boiled meat	50.0 to 100.0	29.0	19.1	0.8	....)	v. Voit.
(Sugar [saccharin]	5.0	0.1	0.02	..	4.8)	König.
Morning (10 o'clock)						
Cold meat / Lean ham	50.0	29.5	19.1	0.9	....	v. Voit.
Rye bread	20.0	8.4	1.2	0.08	9.8	König.
Noon.						
Soup	0. (to 100.0	91.6	1.1	1.5	5.7)	Average of ten different soups according to Reuk.
Roast beef	150.0	87.5	57.3	2.6	....	v. Voit.
(Beef boiled with fat	150 0	85.2	51.5	11.2	4.2)	König.
Salad (green)	25.0	23.5	0.3	1.0	0.5	König.
Vegetables (like cabbage)	50.0	35.5	0.8	0.2	4.2	v. Voit.
Desserts	100.0	45.0	8.7	15.0	28.9	Average of 7 different ones according to Reuk.
Rye bread	20.0	8.4	1.2	0.08	9.8	König.
(Fruit	100.0	85.0	0.3	..	15.0)	v. Voit.
Afternoon.						
Sugar (saccharin)	5.0	0.1	0.02	..	4.8	König.
Evening.						
(Two soft boiled eggs	90.0	66.2	11.2	10.8	0.4)	König.
Roast meat (lean)	150.0	87.5	57.3	2.6	....	v. Voit.
Salad	25.0	23.5	0.3	1.0	0 5	König.
Rye bread	20.0	8.4	1.2	0.8	9.8	König.
Cheese	15.0	5.4	3.6	4.5	0.6	König.
(Fruit	100.0	85.0	3.0	..	15.0)	v. Voit.
Total	700.0	357.0	154.5	23.74	56.3	

Total of water, albumin, fat and carbohydrates which should be taken in the twenty-four hours.

Water	973.0 grams
Albumin	157.6 "
Fat	26 3 "
Carbohydrates	72.8 "

TABLE II.—*Determination of the Kind and Quantity of Food and Drink.*

Fluids taken.	Quantity in grams and centigrams.	Water contained.	Albumin.	Fat.	Carbohydrates in grams.	Analysis after
Morning (7–8 o'clock).			Caffein.			
Coffee	120.0	113.6	0.21	0.62	1.7	König.
Milk	30.0	26.2	1.29	0.96	1.2	König.
Morning (10–11 o'clock).						
Wine (Pfälzer)	100.0	86.1	....	....	2.4	König.
(Or clear soup [bouillon]	100.0	99.1	....	0.8	....)	Reuk.
(Water	100.0	100.0	....	....	....)	
(Port wine	50.0	38.7	0.8	....	3.0)	König.
Noon (1 o'clock).						
Wine (Pfälzer)	250.0	215.3	....	....	7.2	König.
Afternoon (4 o'clock).						
Coffee	120.0	113.6	6.21	0.62	1.7	König.
Milk	30.0	26.2	1.29	0.96	1.2	König.
Evening (after 7 o'clock).						
Wine (Pfälzer)	250.0	215.3	....	....	7.2	König.
Water at discretion	(100.0 (150.0	100.0 150.0				
Total	1000.0	896.3	3.0	3.16	22.6	

Whole quantity of water, albumin, fat and carbohydrates, which are to be taken in the twenty-four hours.

Water	1413.8 grams.
Albumin	169. "
Fat	42.5 "
Carbohydrates	117.5 "

Food taken.	Quantity in grams.	Water contained.	Albumin.	Fat.	Carbohydrates in grams.	Analysis after
Morning.						
Fine wheat bread	35.0 (to 70.0	12.4 24.9	2.4 4.9	0.2 0.4	19.6 39.2)	König.
Two soft boiled eggs	90 0	66.2	11.2	10.8	0.4	König.
(Roast meat	100.0	58.0	38.2	1.7	....)	v. Voit.
Sugar (saccharin)	5.0	0.1	0.02	....	4.8	König.
(Butter	12.0	1 7	0.08	9.9	0.06)	König.
Morning (10–11 o'clock).						
Cold meat Lean ham	50.0	29.5	19.1	0.9	....	v. Voit.
Rye bread	20.0	8.4	1.2	0.08	9.8	König.
Noon.						
Soup	0. (to 100.0	.... 91.6	.... 1.1	.... 1.5	.... 5.7)	Average of 10 different soups according to Reuk.
(Fish [pike]	100.0	74.7	22.1	0.6	0.7)	Boiled in water.
(Vinegar added	25.0	23.5	....	....	0.1)	Loss of water 18% (König).
Roast beef	150.0 (to 200.0	87.5 116 0	57.3 76.4	2.7 3.4	....)	v. Voit.
(Beef [fat] boiled	200.0	113.0	68.3	15.0	0.8)	König.
Salad (green)	50.0	47.1	0.7	1.0	1.1	König.
(Vegetables [cabbage, etc.]	50.0	35.5	0.8	0.2	4.2)	v. Voit.
Desserts	100.0	45.0	8.7	15.0	28.9	Average of 7 different desserts after Reuk.
(Bread [roll]	25.0	7.0	2.4	10.2	15.0)	Reuk.
Fruit	100.0	85.0	0.3	....	15.0	v. Voit.
Afternoon.						
Sugar	5.0	0.1	0.02	...	4.8	König.
Evening.						
Caviar	12.0	6.4	3.0	1.5	....	König.
(Kieler Sprotten	16.0	9.4	3.6	2.4	0.14)	König.
(Salmon [smoked]	18.0	9.2	4.3	2.1	0.07)	König.
(Two soft eggs	90.0	66.2	11.2	10.8	0.04)	König.
Game or fowl Beefsteak	150.0	87.5	57.3	2.7	....	v. Voit.
Cheese	15.0	5.4	3.6	4.5	0.6	
Rye bread	20.0	8.4	1.2	0.08	9.8	
(Fruit	100.0	85.0	3.0	....	15.0)	v. Voit.
Total	852.0	517.5	166.1	39.4	94.8	

tient adapts himself to the diet, and his inclination or aversion as regards fat and carbohydrates, and by the digestibility and availability of these substances in the organism. The albumin given ought to depend firstly upon the albumin of the body. Likewise certain changes can be introduced into this diet scheme so that the allowance of bread, cheese, or fruit is increased, giving altogether an increase of albumin of about 154 grams, fat 45 grams, carbohydrates 102 grams, equal to 1,520 calories, or we may proceed by temporarily allowing instead of these for lunch, 100 grams farinaceous food, with 8.7 albumin, 15 grams fat, and 20.9 grams carbohydrates.

In order not to be compelled to weigh his food daily the patient is instructed to learn to estimate its quantity by certain indications, such as bulk or thickness, measured by taking the size of the hand or other object of familiar size as the standard, telling him to eat a quarter, a half, or an entire roll, a heaped-up or even coffee- or tablespoonful, etc. It will not be found difficult to give the patient proper directions in this regard, and only in this way do we have a sufficient guarantee that the diet is carried out as prescribed.

Von Noorden has recently demonstrated that the amount of albumin of the body can be preserved by a suitable diet favorable to fat reduction. He found by experiment that it is always easier to preserve the albumin of the body if food of a variety to which the patient has been accustomed is employed. The patient, if habituated to a diet of meat, will stand an equally large diminution of fats and carbohydrates, but he who has been used to consume more carbohydrates and less fat will preserve his proper amount of albumin under a marked diminution of fat and an increase in the number of carbohydrates; conversely he who is habituated to much fat and greasy food will remain uninjured by a decrease of the carbohydrates.

A change in the sense of increasing or lowering the one or the other variety of food can always be easily arranged within the limits of the tables given above.

While it is only possible in the most exceptional cases for the practitioner to satisfy himself in regard to the amount of albumin by directly determining the quantity of nitrogen taken in with the food or the quantity of nitrogen in the fæces and urine, he has sufficient indications in the examination of the specific gravity of the blood, its percentage of hæmoglobin, in the increase of the patient's muscular energy, his general strength and sensations of increased vitality and well-being which were previously lacking, and all of these during the slowly decreasing bodily weight. These indications do not only mean the preservation of the amount of albumin but may also show an increase of the latter. If occasionally with these manifestations,

however, a small diminution of nitrogen can be shown by analysis, it is surely only a transitory occurrence and amounts to little so far as the patient is concerned. Practical experiments have established this fact over and over again. The danger of considerable loss of albumin is only present if fat-reduction is carried out incautiously and with too great rapidity, or if the patient gets weak, anæmic, has loss of appetite, indigestion, etc. In this case the attempt at reduction must be changed or given up for a time. The safest means we have, however, at our command of maintaining and increasing the albumin of the body, is the methodical increase of the working power of the muscular apparatus (see below).

Distribution of Meals.

1. *Solid Food.*—In settling upon a given diet we have to divide the solid food, without exception, into small meals or portions. The power of the heart's action and changes in the circulation connected with this power are the factors which determine the manner in which this is done, in order to avoid overdistention of the stomach, the upward pressure of the diaphragm, the displacement of the heart out of its normal position, and an overburdening of the circulation by larger quantities of absorbed food.

The liquids are also to be taken as much as possible at separate times from the solid foods, especially at the principal meals, since meat prevails in all diets, and the stomach juices necessary to digest it must be concentrated and not diluted by much fluid. Soups may be left out altogether since they have no special nutritive value. In the case of an hydræmic and anæmic patient having but a small quantity of albumin, a nourishing breakfast is necessary, and the stomach is not to be distended beforehand or at the same time with tea, coffee, etc., which interfere with digestion, and are injurious by overburdening the circulatory apparatus. Also in plethoric patients who are generally large eaters, it is advisable to distribute the food into small meals, and to let the patients eat frequently in order to break them of the habit of eating too much at a time. These dietetic measures will be further supported by advice to the patient to drink little or nothing during meals, which causes a diminution of his appetite. Instead of three meals, from five to six are ordered and the diet is adapted as set forth, according to the condition of nutrition and the decrease in the fat. According to this diminution of body fat it will be necessary to add more fat and carbohydrates to the diet so as to avoid an undesirable burning up of the body albumin to furnish the necessary calories. If, however, the division of the meals as I have laid down

in the therapy of obesity and circulatory disturbances is carried out too rigorously and the portions become too small (Schweninger), it is possible that the fat-forming substances taken in with these small meals may not be sufficient for the momentary necessities and so may cause a burning up of some of the body fat.

Here, however, the danger is always present that not only an insufficient quantity of fat and carbohydrates but also much too little albumin is taken in with the food. The patient finally eats too little on account of the frequent hourly or two-hourly meals which must of necessity be as scanty as possible, or he loses his appetite from the frequency of eating, all of which not only results in a diminution of fat but also of albumin. A considerable reduction of weight is naturally not to be reached in this manner. This method is nothing more than a hunger cure.

The decomposition of the fat is not at all in proportion to the more or less frequent consumption or absorption of large quantities of food but altogether in proportion to the requirements of the body. If at the time it is required in the economy, too little fat-forming nourishment is taken in, some fat of the body will be consumed, but if it is not then required, even the small quantity of fat or carbohydrates introduced will entirely, or in part, be preserved and be added to the fat of the body. Only where a larger amount is absolutely required than is furnished with the general supply of the fat-forming substance, is a permanent reduction of the fat possible; and it makes no difference whether these fat-forming substances are given and absorbed in numerous but small, or few but large meals. The conditions of weakness frequently observed during these rather stereotyped cures (though Schweninger does not wish to have them designated as cures) are caused by this kind of diet and manner of feeding, and the losses of albumin produced by it.

2. *Distribution of Fluids.*—The distribution of fluids is best arranged after previously having ascertained the varying circumstances in the patient's condition. These experiments are carried out by letting the patient take as much fluid as he is used to for two days and for the following two days diminish the quantity of fluid below the physiological quantity between 750 and 1,200 grams. The fluid which is taken in and the urine secreted are both measured as carefully as possible in graduated vessels. The limit of the day is fixed by establishing a certain hour in the morning, seven to nine o'clock, at which breakfast is taken; all the urine passed immediately before this hour (*i.e.*, before the breakfast) is considered as belonging to the previous day. All that is passed after breakfast and up to the hour of breakfast of the following day forms the amount for one day.

The quality and quantity of solid food must be as far as possible maintained at a uniform figure in order to avoid great differences in the amount of water it contains. In plethoric patients who have normal heart action, and who pass less urine when the amount of fluids taken is diminished, since there is no accumulation of water in their blood and tissues, the fluids supplied need only be limited in proportion to the amount which exceeds the physiological quantity. The burning up of the fat, however, will be considerably increased by diminishing the fluid supply below the physiological measure. In order to accustom the patient to the diminished supply of fluids and in order to prevent nervous excitement, it is advisable not to effect a sudden diminution of fluids (not so, however, where experimental investigations are being carried out), but to do it gradually though not in a protracted manner. A large size of body and a high out-of-door temperature call for a correspondingly larger supply of fluids, as already pointed out.

If the diminution of the fluid supply is followed by an increased excretion of urine as is the case in the hydræmic form, and rarely in the anæmic, taking it for granted that a sufficiently powerful heart action is present, it is necessary to keep the fluid supply *always below the physiological measure* and to diminish it, often to quite a considerable extent. In individual cases, all circumstances bearing upon this being duly considered, it may be fixed at as low a figure as 1,200, 1,000, 800, or even 750 c.c.

The result attained by diminution of the fluid supply together with the burning up of the fat, as in the cases previously mentioned, is often a considerable decrease in weight because the weight of the body is dependent not only upon the amount of fat, but also upon the amount of water in the body.

If hydræmia is proven to be present, through observation and examination (determination of the specific gravity of the serum), and if after the diminution of the fluid supply there is no increase in the secretion of urine on account of a marked insufficiency of the heart, it will be necessary in such case to endeavor to maintain the quantity of fluid supply at a figure which will be fixed by frequent examination, and which will represent the amount producing the largest urinary secretion.

In these cases considerable albuminuria is present and the indication for dietetic-mechanical treatment is of minor importance. Now the weakness of the heart's action and the circulatory disturbances demand medicinal treatment, which will be materially reinforced by the diminution in the quantity of fluid supplied.

I, as well as a number of authors after me, have proven that digi-

talis, which alone would have no effect in such cases, will act, often in a most energetic manner, if a smaller quantity of fluid is taken into the patient's circulation, *i.e.*, if the work of the heart is diminished.

Mechanical Treatment.

Health Resorts.

The mechanical part of the treatment is just as important as the dietetic, in so far as it has to do not only with extensive decomposition of fat accumulated in the body, but also with the preservation and increase in the general amount of albumin present.

The question of the possibility of maintaining the amount of albumin during the reduction treatment has been recently discussed from various sources. In the question before us we must above all not lose sight of the fact that not only the fat but organic albumin is likewise used up by muscular activity, and that consequently the increase in volume of the muscles, *i.e.*, the main fund of albumin of the body, the flesh, depends principally upon the regular activity or exercise of the muscular apparatus. The heart makes in this regard no exception to the muscles of the rest of the body. (See Distribution of fluids.)

The means and methods by which an increase in the muscular work is effected are of several different kinds but by no means of equal value. It is evident that the opinions of authors vary according to their observations, whether made more or less exclusively in a gymnasium by the employment of machines, apparatus, etc., or without these adjuncts simply making use of bodily exercise. In judging of these observations it is easily understood that they are ofttimes not made in a strictly unbiased manner.

Since the object of treatment is not only the diminution of fat, especially in cases of anæmia and hydræmia, but also the formation of blood and muscular tissue, and above all the strengthening of the heart and increasing the volume of its muscular walls, which are in a state of fatty infiltration, atrophic, and functionally insufficient, it follows that increased muscular power is not exactly caused by a large amount of work in itself, which besides might be the cause of dangerous conditions, but rather by the length of time during which the muscles are active. This manner of increasing muscular strength is the rule in all cases of debility of heart action. It is not sufficient that the patient goes through with a gymnastic exercise or active work for an hour or an hour and a half a day, because the amount of muscular work is too small to produce the necessary decomposition of the fat, and furthermore activity concentrated in this limited period, that is to

say, intense muscular exertion kept up for a short time, is apt to carry with it the danger of overtaxing the heart. If we are to expect successful results from our therapeutical methods muscular activity must be extended over at least four to five hours daily, best in the morning and afternoon hours. The reason for this is that the muscles are better nourished and absorb more of the food supply in direct proportion to the length of time muscular action is continued. If, as some authors claim, the success of the treatment for obesity is to be expected only after a long period, say a year, and if the patient is supposed to lose but a few pounds within such a time, it is no longer worthy of being called a therapeutical measure. The method to be chosen must make it possible to increase the muscular activity gradually from the least to the most intense exertion, either slowly or quickly covering the necessary period. The two indications in question, *i.e.*, the decomposition of the fat and the preservation and increase of the albumin of the body, are best met by exercise which consists in walking and climbing in open-air health resorts.

Such places make it possible to increase the exercise from a simple walk on the level for a certain length of time up to the climbing of paths having an incline of twenty degrees; beginning with a few steps and gradually increasing to an hour's walk each morning and evening.

For those health resorts I have selected different places in various climates in order to permit of treatment being carried out at all seasons, such places being chosen as offer the advantage of proper lay of the land for the walking and climbing exercises. These "health paths" are located partly in the plane, partly winding about hills, and are divided into four categories:

Paths of the	first	order with an incline from	.....	0°	to	5°
" "	second	" " "	.....	5°	"	10°
" "	third	" " "	.....	10°	"	15°
" "	fourth	" " "	.....	up to 20°		

The paths themselves are divided by columns, wooden poles and other signs into distances corresponding to fifteen (sometimes ten) minutes' normal walking time. This manner of dividing the path is absolutely necessary for measuring the amount of muscular exercise prescribed. If we let the patient measure the exercise by the watch, the work done will rarely accord with the patient's strength and will not meet the indication of the given case.

The lazy and indolent patient will limit his exercise to the shortest possible walk and do but imperfect and unsatisfactory work, while the overzealous walks or climbs in the same time possibly twice as much as is good for him, and thus overexerts himself.

By dividing up the paths in the way described we can regulate the mechanical element of treatment in the most accurate manner, and at the same time, in the individual case, we may increase the work according to the indications, such as the state of the heart's strength and of that of the general muscular system, by advising a walk on an incline from 0 to 15° and 20°, and from a short time up to a number of hours.

At these health resorts the paths are marked by differently colored signs; the level paths are indicated by red, those having slight incline by blue, and those of greater incline green or violet, and finally those of the largest admissible incline yellow. The time (10 to 15 minutes) is indicated by marks. There are a number of these resorts in Germany, Austria-Hungary, and Switzerland.

Patients who have already visited other regional health resorts and have some experience in gymnastic treatment may carry out a "terrain" cure also at Ischl and at various other places in the Salzkammergut and the Bavarian Alps. The measure of exercise to be performed may be regulated with a pedometer instead of in the way mentioned, but only if the patient has a good instrument at his command, which is not always the case. The so-called pedometers are mostly unreliable and fail to register, say, one hundred steps out of a possible one or two thousand, or else they record as a step the slightest movement of the body. In using these instruments on certain inclines they must always be carefully watched and controlled.

Distribution of Work.

The work is distributed according to the force of the heart, the state of nutrition and strength of the patient, the character of the affection, whether of the anæmic, plethoric, or hydræmic form, and the complications.

1. If the force of the heart is sufficient and a plethoric condition is present the patient may be allowed from the beginning to take walks of the first and second varieties, viz., those having an incline of 5 to 15 degrees, and he may be permitted to pass over six to eight units of distance, the return course not being reckoned in, and the exercise may be distributed over the morning and afternoon hours according to circumstances.

Taking normal walking time as a standard, this work of six to eight distance-units would require, including going and coming, three to four hours. The patient himself can employ as much time as necessary for this, and his attention should be called to the point that it does not matter how long he takes to cover the distance, say,

of six units. The main point is that the work is done. Later on the work is increased or, according to circumstances, decreased, from time to time. Days of rest may be interspersed in order to protect against over-exertion.

Paths of the fourth order up to 20 degrees can only be made use of from time to time, in case the heart is perfectly strong and the general condition has been so far brought back to the normal that it insures the preservation of the heart's force. The patient must be impressed, no matter what curative walking exercise he takes, not to hold the breath, but to breathe in and out deeply and quietly. If he gets short of breath during the walk he is to adapt his gait according to the capacity of his lungs, a step being counted to each inspiration and expiration. It is also admissible for the patient to breathe during a short time, say for five minutes, when he is walking on paths of the second or third order, in an interrupted (*staccato*) way; that is, to follow an inspiration by two expirations in such a way that, for instance, two steps coincide with one inspiration and two steps with two expirations; in this broken manner of breathing perfect expiration is secured and also thorough inspiration. At the same time the two expiratory efforts, if they are somewhat intensified, exercise a certain slight pressure effect over the heart's surface, which, received and collected by the heart action, has the effect, as it were, of an invigorating massage to the heart muscle.

2. If the heart action has become more or less impaired, as is the case in the anæmic and still more in the hydræmic form, it is best to begin with paths of the first and second order and to prescribe according to the general conditions present four to five lengths of distance, more on the level and less on the incline, and slowly to increase the work in proportion to the strength gained, up to six and eight distance-units. In these cases, more than in those previously discussed, the greatest attention must be paid to the manner of breathing. If air is not freely enough admitted through the nose, thus doing away with the frequent difficulty of respiration often coming on suddenly, the patient must breathe with open mouth and bring the efforts at breathing into rhythmical relation with the pace. One to two steps must correspond to the inspiration and the same number to the expiration, or, if interrupted breathing is for a time resorted to, with two expirations, and the latter must be performed with a little more force. Only *after a longer period*, two to three weeks, according to the severity of the case, and under the condition that the heart muscle is sufficiently accustomed to the exercise and properly strengthened, the paths of the third order (up to 15° incline) are to be chosen. The paths of the fourth order will either not come into requisi-

tion at all or will be used only in exceptional cases where the patient is to be considered as in perfect health. After a year or so these paths may be used more frequently by those who were formerly under treatment, and these patients may also try mountain climbing. Here, more so than in the previous class of cases, muscular work must be regulated so as to be spread over a more extended period and to correspond with the patient's strength, being gradually increased. Aside from an increased burning up of the fat there must be an increase in the albumin in order to enhance the development of blood and muscles, and to favor the processes of nutrition and growth. This is done not alone by augmenting the albuminous food, but rather by strengthening the muscles and making their action more effective. The strengthening of the heart and the development of all the other muscles of the body take place in the same manner by reduction of the fat deposited upon and interspersed between their fibres. These changes in nutrition finally result in a clearly demonstrable decrease in the dilatation of the heart. The percussion dulness of the heart may also be diminished by atrophy of the fat and by more powerful contraction of the strengthened heart muscle.

3. Sclerosis and atheroma of the vessels form the most dangerous complications in respect to mechanical treatment; affections of the coronary artery and its branches and of the arteries of the brain are the most serious. Where the development of a sclerosis is to be dreaded, possibly on account of hereditary disposition, a uric-acid, atheromatous, or gouty diathesis, we must try to counteract these affections as early as possible. Besides the ordering of a suitable diet and limiting the use of alcohol, we have in *walking and climbing* exercise a powerful remedy to stimulate the nutrition of the vessels, and the elasticity and contractility of their muscular elements. This constitutes, as it were, a gymnastic exercise of the blood-vessels.

After walking for a certain period, especially climbing mountain paths, the arteries dilate, become distended, while the increased blood-pressure removes all existing stasis, a condition which may remain not only for the few hours during the exercise but also for ten to twelve hours and more after it has been accomplished. Consequently in such cases as do not yet clearly show arterial changes, paths of the first, second, and third order according to the rules and cautions laid down, may be advised, always taking into account the state of nutrition and the power of the heart action. If, however, sclerotic changes of the arteries have already become established, if sclerosis can be demonstrated or is probably present, the walking exercise and climbing must undergo further restrictions, in which case the rules

given under 2 have to be modified so that in the beginning especially, every marked increase of the blood pressure is avoided, so that only paths of the first and second order are used, and so that exercise is limited to rarely more than two to four units of distance. Later on if the heart force has improved, and there is no palpable increase in the sclerotic condition, paths of the third order may be resorted to and exercise may advance to several units, especially on level paths or those of slight incline. If atheroma of the blood-vessels has developed, the walking and climbing exercises must be regulated more cautiously and limited to paths of the first and second order and to a small number of distance units. In no case, however, should exercise be altogether dispensed with.

The minutest precaution is indicated in sclerosis of the coronary arteries, whether this affection is only supposed to be present or whether stenocardic attacks have already occurred. In regard to exercise in these cases the smallest amount, taken on almost exclusively level paths, is to be advised, but it is to be altogether forbidden only in exceptional cases where there are frequently recurring attacks, since with absolute rest, disturbances of nutrition and circulation, those of the heart included, will soon grow worse and induce a condition of weakness; this is not the case if the muscular apparatus is kept active. If *myocarditis*, a *pronounced albuminuria*, and general *œdema* have already appeared, while the insufficiency of the heart muscle has gained headway through sclerotic changes, *rest* and *medicinal treatment* alone are capable of preserving the patient's life for some time. Likewise if symptoms from the side of the brain have shown themselves along with sclerosis and atheroma, congestive conditions, dizziness, if apoplexy is threatening or a cerebral thrombosis or hemorrhage has already occurred, a strictly mechanical treatment by walking and climbing exercise is best dispensed with. The treatment will then aim at stimulation of nutrition and circulation by ordering short walks on the level which, under these conditions, will in nowise endanger the patient.

The presence of diabetes mellitus does not modify the rules of mechanical treatment (see below).

Finally as regards the time of day at which the cure-walks are to be undertaken, the morning and late afternoon hours are those best adapted to the purpose, because the stomach is least filled at these times and digestion has already progressed to a certain extent. Immediately after a hearty meal a walk must never be undertaken, nor must the patient perform any other kind of bodily exercise. After the noonday meal he must rest for an hour, including, possibly, a quarter to a half hour's nap.

Muscular Exercise of Other Kinds.

Muscular work without the advantage of adapting it rigorously to each particular case, may of course be prescribed in various other ways, but all methods aiming at this are inferior to walking and climbing at special health resorts (Terrain Curorte). They are most admissible in those cases in which a visit to these health resorts, or walking and climbing exercise is not practicable for one reason or another. I have pointed out elsewhere the insufficiency of Swedish gymnastics by figuring out the greatest decomposition of fat in the time set down for these exercises based upon observations upon forced muscular work (Pettenkofer and Voit). Practical experience in using these methods agrees perfectly with the computations which have been made. The decomposition of fat which is thus accomplished is too insignificant and insufficient when we consider what an immense amount of fat has to be done away with. The results are better from the *working machines* (Gaertner's ergostat). The apparatus consists in a turning wheel which is balanced by a weight fixed to a lever and which offers resistance to efforts at turning according to the weight attached. The motion of the apparatus depends upon the position the patient assumes while working it. When disturbances in the circulation and respiration are present, such as heart insufficiency, stasis in the venous system, as is the case in obesity with fatty heart, especially in the anæmic and hydræmic class of cases, the slightest upward pressure upon the heart and lungs will cause dyspnœa, making it impossible to employ the apparatus without injury to the patient. Even if the latter assumes different positions from time to time, which according to Gaertner must correspond to the various phases of respiration, it will make no difference in the result. The apparatus can only be used in the first stages of the plethoric form if the heart is still intact.

The same limitations concern likewise *other methods of work*, such as sawing and splitting wood, rough games, dumb-bell gymnastics, etc. These can only be used in cases where the heart is still capable of normal effort, and where dilatation of the heart from excessive work is not to be dreaded. This concerns again cases of plethora in the first stages of obesity, but even here the work done must be under the constant supervision of the physician, and the patients must never be lost sight of for too long a period, since just when treatment is being most efficacious, if a rapid decrease of fat takes place, over-exertion of the heart may easily occur. In this connection I want to call attention to the fact that by increasing muscular activity alone without suitable diet (Bunge), fat reduction is not

readily brought about (Banting), and in those cases where nevertheless an occasional effect has been observed, it was after all due to a diminished ingestion of fat-forming substances and the burning up of the stored body-fat, factors which may have escaped observation.

Accessory Measures and Procedures.

Other measures in the treatment of obesity, such as removal of tight and laced articles of dress, cold ablutions, frictions, sponging of the breast and abdomen, arms, legs, and buttocks, and hot foot-, arm-, or head-baths—in short partial applications of cold and heat (Schweninger) are only to be considered as of some sanitary and hygienic value, but not as having the slightest influence upon fat reduction.

The decomposition of fat accomplished by regulating the warmth of the body (Rubner) as by the cold-water bath or steam and hot-air bath, is very slight and of no essential value.

Self-applied massage, as in pressing, kneading, pinching of the abdomen, breasts, hips, buttocks, etc., has been recommended, but such mechanical treatment can have no effect whatsoever upon the circulation as is claimed, nor will it produce the slightest decomposition of fat. At best a partial dilatation and contraction of the blood-vessels is brought about by the mechanical irritation; this, however, produces no marked influence upon the general circulation nor upon the process of fat-reduction. The muscular work which is performed by the patient while he kneads, pinches, and rubs himself can alone be of any benefit in securing reduction, and this again can only be estimated as of minimal importance.

Attempts to explain the changes by employing the phrase "*stimulation of metabolism*" (an expression which was coined to explain and elucidate everything and which is supposed to mean stimulation of local and general circulation) are entirely without foundation, since these procedures influence everything else except the processes in question.

Balneological and Hydrotherapeutical Treatment.

The springs, so popular for ages, which yield cold alkaline and saline waters, such as Marienbad, Tarasp, etc., and which contain beside sulphate of soda, bicarbonate of soda in large quantities, cannot be considered specifically efficacious in the treatment of obesity, a resulting decomposition of fat not having as yet been demonstrated. Cures with these mineral waters can only be looked upon as adjuvant to dietetic and mechanical treatment in the first stages of obesity,

abdominal plethora, and chronic stasis of the large intestines. After the use of Glauber's salts and other salines the cathartic action of which consists principally in exciting intestinal peristalsis, the fæces contain, according to Radziejewski's experiments, large quantities of *peptones* from the small intestine and of *fat*, and indeed in much larger quantities than is found normally. These substances escape digestion and absorption because of the excessive and violent peristalsis, and are thrown off without being made use of. The *cures* at Marienbad, Tarasp, etc., are in consequence essentially *starvation cures*, which prevent part of the nourishment from being used in the economy. Obese patients with anæmia and hydræmia, whose quantity of body albumin has already suffered loss, and who no longer consume an excessive quantity of food, always do badly under the *process of throwing off* unused food substances containing both albumin and fat-forming material, and the conditions of weakness promptly setting in prevent a continued extensive use of these mineral waters.

The cathartic mineral waters are only to be used in cases where a slight starvation cure can still be well borne, as in the plethoric form of obesity affecting individuals who are accustomed to the pleasures of a rich table with great variety of dishes and of drinks, and who have developed a chronic dilatation of the stomach and intestines. The discrepancy between supply and waste in these cases is corrected by the laxative action of mineral waters. The surplus taken in by the mouth leaves the body unused, per anum. The action of the mineral water may be likened in its effect, *mutatis mutandis*, to that of the peacock feather used by the ancient Roman in his banquet feasts. The diet employed during these mineral-water cures, which aims more or less at a diminution of fat-formation and is far inferior in quantity to the excessive diet of obese persons in general, suffers a further reduction through the alkaline and saline waters, and nutrition is correspondingly diminished.

Of advantageous influence, however, is the action of the waters mentioned above, upon the abdominal plethora existing in these cases, upon the stasis in the portal circulation, in the hemorrhoidal vessels, and in the disturbances of the stomach, intestines, and genito-urinary apparatus, referred to in the chapter on symptomatology. The success which may follow is often very decided and is increased furthermore by a combination with walking and climbing exercise, or better, by a "terrain cure" strictly adapted to the power of the heart's action and the general strength of the patient.

We can sum up the indications for mineral-water cure briefly by stating that they are only to be recommended in the *first stages* of

obesity of *plethoric* character, in disturbances of the portal system, and in advanced cases where these disturbances prevail.

In order to accomplish the above result it is *absolutely requisite* that the mineral water should not be retained in the system, but that it quickly produce emptying of the bowels and is thus eliminated. Therefore if catharsis does not take place the two other therapeutical effects, as pointed out above, are obviously excluded; now comes into consideration, on the other hand, the influence of increased fluid supply upon the heart and vascular apparatus as well as the effect of the sulphate of sodium contained in the water upon the blood.

It is therefore always necessary to regulate *the quantity of the mineral water exactly according to the result of experimental research* and to subtract it from the total amount of fluid which the patient may be allowed. Experimentation will demonstrate whether disturbances of circulation have taken place through the inability of the vascular system to accommodate itself to the fluids taken in and to excrete the same.

A course of mineral water doubtlessly yields better results if carried out at a watering-place than if attempted at home under the usual conditions which have been only slightly changed. At the resort the patient not only takes his daily quantity of water regularly as prescribed, but the diet also is perfectly adapted to the treatment. Furthermore example and the disquieting stories in circulation among the guests concerning the bad consequences, for instance, catarrh of the stomach and intestines, colics, diarrhœas, and other distressing conditions caused by overloading the stomach, prevent even the gourmands who are accustomed to a bountiful table from trespassing beyond the prescribed diet limits.

Likewise there are provided at these places walks, and the strict advice of the physician and the emulation of the patients among themselves induce even the easy-going and lazy patient, in the majority of cases, to perform sufficient bodily exercise to reduce his weight by a few pounds at least.

Since the patient, after having gone through a mineral-water course, relapses into the old routine life, it is necessary to repeat the cure, as a rule, the following year.

After some years, however, disagreeable consequences follow either gradually or suddenly with the usual decrease in weight of greater or lesser extent. After a limited use of the strongly cathartic mineral waters, which cause the albumin as well as the fat-forming substances to leave the intestinal tract without having been of use in the economy, the patients feel extremely weak and debilitated. The physician as well as the patient himself under these circumstances be-

comes afraid to continue treatment in the usual manner. Changes are made in the quantity and quality of the mineral water, and after a time their use is entirely given up and some other method of treatment is tried.

The reason why this peculiar change takes place during a course of mineral water, lies in the transition of the plethoric form into the anæmic and hydræmic, which means a considerable decrease in the amount of albumin of the body, a growing insufficiency of the heart, and an accumulation of water in the blood and tissues. If in such cases the cure is continued in spite of these warning symptoms, dropsy will soon develop and the life of the patient will be immediately endangered.

For the *anæmic form* of obesity the indications have also been formulated—the use of slightly cathartic mineral water containing at the same time a certain quantity of iron. For instance, the waters at Franzensbad, Tarasp, Kissingen, Wiesbaden, Cudowa, and others. The success which has been noted following the use of these waters is not so much due to the tonic effect of the iron in the water as to the general dietetic *régime* carried out at such resorts.

Besides these, many other both natural and artificial iron waters and iron preparations are made use of: the waters of Levico (weaker and stronger springs), Roncegno, the Guberquelle (containing iron and arsenic), pyrophosphate of iron water, etc.; Blaud's pills, ferri albuminas and ferri manganas, the hemalbumin and hæmoglobin preparations, and still others.

Hydrotherapy is often employed in the treatment of obesity. The real benefit derived from cold as well as from hot steam baths is very slight, according to the experiments of Rubner made upon the regulation of heat, and especially in reference to such baths. I have pointed this out in my "General Therapy of Circulatory Disturbance," 4th edition, p. 320 *et seq.* With cold baths of 15° C. and of a quarter-hour duration (the extreme possible limit), 10.7 grams of fat are decomposed (Rubner) and this figure is increased to 19.7 grams through the cooling-off process and the after-effects. Ten baths of a half-hour's duration each will only decompose 394 grams of fat, and in order to use up four kilograms of fat one hundred such baths would be necessary, provided any one could stand such continuous bathing. This shows the slight effect of such baths where we have to deal with a body weighing from 110 to 120 kilos (240 to 260 pounds) and over. In steam and hot-air baths decomposition of fat is at any rate so slight that they have practically no therapeutic value. The great loss of weight noted after such baths has for its explanation, according to Rubner's and my own experiments, the extensive loss of water during

the sweating in the baths. Cold baths are, however, to be made use of as adjuvant, stimulating, and generally invigorating means. They may be so combined with the terrain cure, *i.e.*, the fat-reduction through walking and climbing exercises, that the time of the after-effect of the bath is made use of for such exercises. At this time, the regulation of body heat and the whole circulatory apparatus are under the influence of the cold water just used, the effect of which is added to that of the terrain cure. The action of the heart has been strengthened by the thermal stimulation. The heart beats slower, the blood is driven into the dilated network of peripheral arteries under a stronger impulse and remains longer in the cool skin (Winternitz).

Dry warm-air baths, hot-air baths, and Roman baths are principally to be used in anæmic and hydræmic cases in order to reduce the amount of water accumulated in the blood and tissues. They must be employed in combination with a decrease in the supply of liquids as mentioned above. Steam baths are not so well suited to obese patients with circulatory disturbances, since the air saturated with steam frequently interferes with respiration and causes dyspnœic symptoms and asthma. The number of Roman baths allowed ought not to exceed three per week. The patient remains under constant observation of the physician and undergoes frequent examination. Threatening symptoms from the side of the brain, the respiratory, and the circulatory apparatus obviously contra-indicate the use of these baths.

After-Treatment and Subsequent Mode of Life.

After the masses of fat accumulated to excess in the body have been burned up and the normal condition between the albumin and fat has been re-established, there remains the further task of preserving for the future the condition which has been attained.

The means and methods, especially the mode of life through which the patient has regained his normal state, must be kept up in their general outlines, and everything must be removed which might favor renewed accumulation of fat. The rules according to which the former patient must regulate his life consist, as did the treatment, in proper nourishment, *i.e.*, diet, muscular activity, exercise, and finally regulation of the amount of fluids of the body.

a. Diet.—This has to be regulated in general according to the form of obesity previously treated, whether the plethoric, or the anæmic, or the hydræmic form, and it must agree with the former diet under which the patient recovered. In the plethoric form the

amount of fat and carbohydrates must be kept within a certain limit, while albuminous food must form the bulk of the meal. The amount of fluid taken in may vary between 1,500 and 2,000 c.c. according to the condition of the circulatory apparatus. It ought, however, to contain little alcohol, sugar, or malt. Strong wines are prohibited and but little beer is allowed. In the anæmic form, where danger of a loss of albumin is still present, carbohydrates together with a sufficient diet of albumin may be allowed in a somewhat larger proportion, since they greatly favor the preservation of the latter. On the other hand the amount of fat taken should be small. The list of liquids, which in women should never exceed an amount representing 1,200 to 1,500 c.c., can include strong wines and beer in small quantities, according to the state of nutrition and general condition of strength. They should be limited in amount or entirely omitted if the patient's state of health no longer requires them, or a sufficient formation of fat makes itself noticeable.

If hydræmia has already been in existence and if a loss not only of albumin but also of fat has occurred, fat as well as carbohydrates have to be admitted to the diet list, but only to such an extent that the patient never takes an insufficient amount of albuminous food.

In sclerosis, either already present or threatening, alcoholic beverages must be avoided as much as possible and allowed only temporarily in adequate amount where there is indication for the employment of stimulants. The amount of fluid taken must be limited to the smallest quantity, 1,000 to 1,500 c.c., and is best regulated according to the results of experimental research.

Distribution of Diet.—According to my experience, which is the result of many years of observation, I will give the following general rules as regards the distribution of the diet, without anticipating rules for the individual case:

Morning: A cup of coffee or tea with some milk, 150 to 200 c.c., and 75 grams of bread.

Forenoon: In cases of preceding anæmia and hydræmia one to two soft-boiled eggs or thirty to forty grams meat, cold or freshly broiled, 100 c.c. wine (in conditions of weakness, 50 c.c. of port wine, and a little bread).

Noon: 100 c.c. soup; 150–200 grams meat of various kinds, variously prepared boiled or broiled beef, veal, game, or fowl not too fat, salad or easily digested vegetables at discretion; likewise fish cooked without much grease, 25 grams of bread or some other farinaceous food, at most 100 grams; for dessert fruit 100 to 200 grams, best fresh or preserved (especially after Naegeli's method). For drink $\frac{1}{6}$ to $\frac{1}{4}$ litre of light wine or beer; some water.

Afternoon: Again 150 to 200 c.c. coffee or tea with about ¼ litre of water, bread about 25 to 50 grams if there is a desire for it.

Evening: Meat as above, or eggs, 25 grams of bread, possibly a little cheese, salad, and fruit. Beverages: Wine, with or without water, or beer, best taken some time after the meal, up to 300 or 500 c.c. Delicacies, oysters, caviar, etc., by reason of their nourishing qualities, may be eaten before or between meals, but so that they do not too much augment the total quantity of the food.

b. As to what concerns the second object of treatment, viz., *the preservation of the heart power, accumulation of albumin,* and the *burning up of the superfluous fat,* the patient after recovery has still to pay special attention to exercise of the body and gymnastics: daily walks of an hour or more must be undertaken. In the spring, summer, and fall months he must visit a terrain cure resort or some other place with hilly surroundings, where it is possible to use paths of the proper incline such as he has become acquainted with from his previous stay at a terrain resort. In winter or in unfavorable weather gymnastics performed in the various institutions, home gymnastics, or Swedish movements, work with the ergostat, splitting of wood, etc., must constitute the mechanical treatment. It must be left to the physician to regulate and watch the work.

c. Where the circulatory apparatus has suffered to a considerable extent, where congestions of its venous portion have made their appearance and entire compensation has not been effected, the regulation of the amount of fluid taken in and the amount of urine excreted must be carefully watched by the patient after his recovery. Experimental researches comparing the amount of fluid absorbed with that of the amount of urine secreted must be undertaken from time to time.

If the danger of a large accumulation of water in the blood and in the tissues reappears, it must at once be met by prophylactic and curative measures, consisting in diminution of fluids allowed and in stimulation of excretion, by encouraging perspiration, by advising climbing exercise, Roman baths, Russian baths, or by the hypodermic administration of pilocarpine.

Treatment of Lipogenous Diabetes Mellitus.

The chief principle in the treatment of diabetes is to protect the patient against the loss of albumin. If he has not as yet been reduced in fat, *i.e.*, if the glycosuria has been discovered early enough, the preservation of the proportion is easier than it is later on when he has already lost much flesh. By putting the patient on a purely

nitrogenous diet it is not possible even in diabetes to keep his body in a condition of nitrogen-equilibrium. Purely nitrogenous food, meat diet, 500 to 1,000 grams, can only be kept up for a short time because the patient not only soon becomes disgusted with it, but also is scarcely ever able to eat meat enough to prevent further decomposition of body albumin; or dyspeptic symptoms appear, catarrh of the stomach and intestines necessitating an absolute change of diet.

As in the treatment of obesity the preservation of albumin is closely connected with the taking in of fat and carbohydrates, and the patient has to take a sufficient allowance of both even in face of the danger that an increase of carbohydrates may also increase his glycosuria. In cases where fat does not well agree with the patient and he has a strong desire to consume large quantities of the carbohydrates, such are best supplied to him as contain a large proportion of indigestible cellulose, as, for instance, potatoes and black bread, the use of which allows of a further introduction of sufficient butter or other fat; 200 grams of potatoes and 100 grams of black bread correspond only to 100 grams of carbohydrates of which furthermore only about 90 grams are digested and absorbed.

Where the desire for carbohydrates is not so pronounced we can better choose those carbohydrates which take up but a small volume, and permit instead large quantities of nitrogenous food, meat, fatty meat, sausages, and eggs. At the same time bread, cakes baked with levulose, aleuronat bread, etc., can be given.

Where there is no complication through disturbance of the appetite, and no disinclination for a preponderance of food rich in albumin, it suffices that the meals have a composition, taking cognizance of the individuality in each case, as is indicated in the diet tables I. and II. already given.

A mode of living adapted to the special case must be adhered to for a long time, often even for years, and can be changed only in case of modification in the nature of the disease, the state of nutrition, and complications arising.

Muscular activity, walking and climbing, exercise at the terrain cure resort, gymnastics, etc., must be brought into requisition not only to encourage burning up of the fat but also to oxidize the sugar and to maintain the strength and substance of the muscles. If diabetic coma is threatened we must exhibit large amounts of carbohydrates in order to retard the decomposition of albumin which occurs rapidly. It still requires careful observation to determine in how far we can accomplish this result.

Medicinal treatment for diabetes does not exist. Mineral-water cures and dietetic treatment in Carlsbad often work favorably and

we would not hesitate to let the patient go through the course of treatment at this resort if it seemed otherwise indicated.

Medicinal Treatment of the Complications and the Final Stage.

There is in reality no such thing as a medicinal treatment of obesity. Only a number of intercurrent concomitant and dependent symptoms and complications, as well as those serious and hopeless conditions which usher in the final stage and continue until death, call for medicinal treatment.

The intestinal symptoms, accumulation of ingesta, persistent constipation and coprostasis, congestion of the portal system, require the use of more or less active cathartics. Here belong the various salts—Glauber, Carlsbad, Marienbad, which are to be taken in tablespoonful doses in a glass of water, morning and evening. Furthermore rhubarb, aloes, jalap in powder or pill form, cold infusions of senna leaves (deprived of the resinous substances), castor oil, preparations of cascara sagrada in wine, tablets, or pill form, frangula, tamarinds, and still others. These medicines can be intensified in action by a liberal supply of water in injections, or injections of cathartic substances or glycerin, massage, or electricity.

Particular attention must be paid to intercurrent febrile disease. Since the loss of heat from the surface of the body caused by cooling off, or a cold bath, is less in obese patients than in others, the use of antipyretics by the mouth in requisite amount must supplement these therapeutic measures, with the proviso, however, that they do not weaken the heart. Any further modification of treatment is not indicated by the presence of obesity. We have only to carefully observe the condition of the heart in each affection and every phase of it, and all therapeutic measures must be regulated according to the existing strength of the heart.

Cold ablutions, cold rubbings, local baths, sitz baths, and other hydrotherapeutic procedures are furthermore indicated by the skin diseases dependent upon obesity, and exercise a favorable prophylactic as well as curative effect.

Eczematous inflammatory processes, seborrhœa, require medicinal treatment on the one hand by dusting powders made from lycopodium or finely powdered starch, to which benzoin and rose oil may be added, dermatol, salicylic acid, tumenol, etc. Or, on the other hand, in a more serious eczematous condition, astringent salves of lead or zinc preparations, white precipitate, ichthyol, calomel, solutions of boric acid, tannin, sublimate, emplastrum diachyli Hebræ, and others.

More advanced degrees of seborrhœa which cannot be removed by simple lotions will furthermore be favorably influenced by alcoholic or ethereal solutions, eau de cologne, etc. These ingredients dissolve a part of the sebum and thus remove it.

For pruritus the best remedy is tumenol sulphone, 1 to 20. If arteriosclerosis has developed, medicinal treatment is unavoidable aside from the dietetic-mechanical treatment which has to cope with this affection. For affections of the arteries sodium iodide, in doses of 15 to 30 grains per day, may be tried. This remedy alleviates furthermore the attacks of dyspnœa and asthma caused by the sclerosis. If uric-acid diathesis is present at the same time the alkaline waters, carbonate of sodium and lithium, the waters of Salzbrunn, Oberbrunn, Wildungen, Bilin, Fachingen, the Salvator Spring, Carlsbad, Mühlbrunnen, Vichy, Célestine are indicated, and their administration has to be regulated according to experimental researches which are first to be made in order to find out the amount of fluid which, when taken, produces the most extensive secretion of urine.

In cases of stenocardiac attacks nitrite of amyl 3 to 5 drops, nitroglycerin in solution (twenty drops of a 0.3 per cent. to 1 per cent. solution in 6 ounces water, three tablespoonfuls daily, or tablets each containing 0.0005), nitrite of sodium (gr. xxx.— ℥ iv., three teaspoonfuls daily, the last to be taken in the evening) will often give the patient ease. If these should disappoint in action, small doses of morphine subcutaneously applied (gr. $\frac{1}{8}$) will remove the painful condition or at least make it bearable. Mustard poultices, dry cupping, or the application of a hot-water bag over the heart region may abbreviate or alleviate the attack. If sclerosis and atheroma of the arteries of the brain have caused thrombosis and rupture of a blood-vessel (apoplexy), the treatment conforms to the gravity of the symptoms according to the localization and severity of the injury, following the lines of special therapeutics.

Should the heart weakness increase in the further development and final stage of the affection, and the ever-increasing dilatation fail to be compensated for by hypertrophy, and if œdema sets in, then the medicinal treatment with digitalis, strophanthus, and other heart remedies should be once more tried, especially after decreasing the amount of fluids taken, since these remedies are almost always more energetic in their action when administered in this way. Compensation may thus be started or the ever-increasing circulatory disturbances may be held in check.

If one is no longer successful, or only imperfectly so, if the dropsy grows worse, and ascites, hydrothorax, and hydropericardium come on, we still almost always get good results in the beginning by the

use of diuretics or by employing surgical means, by tappings, scarification, or the introduction of small trocars into the greatly swollen extremities, thus ridding the tissues of the accumulated fluid, and relieving the patient for a considerable time; but at last these measures fail us too.

Should œdema of the lungs or paralysis of the heart make their appearance we may make local counter-irritation by mustard leaves, mustard hand baths, dry cuppings, and give internally ether, brandy, liquor ammoniæ anisatus, musk, castoreum, camphor by the mouth and hypodermatically (oleum camphoræ). In this way we may postpone the catastrophe for a while until finally in the next attack or the next one after that death releases the sufferer from his deplorable condition.

Results of the Dietetic-Mechanical Treatment.

If this dietetic-mechanical treatment of obesity, even in the advanced stages of the disease, but not in the final stages, is carried out according to the above rules, the result is without exception a cure, or in advanced degeneration or irreparable organic changes, the securing of the very best possible condition. If the treatment is directed according to the individual case, no further disturbances, and especially no fainting spells and no nervous excitation will appear. The physician has the whole process of fat-reduction well in hand and can regulate it, retarding or hastening it as the conditions present indicate.

Since a too quickly progressing fat-reduction and decrease in the quantity of body albumin may favor inanition and conditions of weakness, it is recommended that the fat consumption be carried out slowly and not too extensively. Where at the same time an abnormal collection of fluid in the body, *hydræmic* and *serous plethora*, is present, the danger that the condition which at first was but a latent hydrops will be transformed into the actual disease, will be avoided by decreasing the amount of fluids taken in and increasing the excretion of water from the body.

This danger is all the more liable to occur the more the amount of fluid taken in is unrestricted, and it is even worse if the quantity is increased while the heart power is insufficient and the excretion of urine is diminished.

As the reduction process advances, especially where fat and water in the body are reduced at the same time, the *habitus* and the appearance of the patient change. In cases of plethora in young patients and those having hereditary predisposition, loss of weight and

bulk takes place but slowly, and the skin filled out by the masses of fat is still in a condition to shrink over a limited surface. The circumference of the patient's body will be decreased in all its parts; he will usually appear younger in looks, but in rare cases older. If, on the contrary, the obesity has existed for a longer time, and has led to anæmic states, and to accumulation of water in the blood and in the tissues, and if the patients are in advanced life, and have a bloated appearance, with fatty masses presenting a flabby and doughy instead of a firm and solid feel, and if the loss of weight, especially that due to abundant excretion of water, has been rapid and marked, the patient will seem to be debilitated and he will impress one as being ill on account of his flabby skin which is little or not at all reduced in extent of surface, is pale, anæmic, and frequently covers in loose folds parts of the body which have become considerably reduced, especially over the face and neck. On the other hand the patient feels himself in reality at last freed from his previous ailments, his circulatory disturbances which weighed him down, the heart is stronger and the dyspnœic oppression comes now seldom or not at all, and the ability to work reappears in conformity to his age, often in a most unhoped-for manner. Thus it may come about that the patient's friends worry and pity him on account of the contrast he presents compared with his former condition, when, though suffering considerably from the far advanced circulatory disturbances, he was envied for his fat appearance and his ruddy complexion (which was, however, really more cyanotic) and was believed to be in good health.

The disappearance of such changes in the habitus and looks and the harmonizing of these with the actual normal or almost normal conditions of health can only be effected after a longer period, not infrequently requiring half a year to a year. If the disease be so far advanced that medicinal treatment has to be resorted to on account of life-threatening conditions, there is no longer room for the treatment of obesity.

The result of combating these conditions depends then only upon slight palliative action of the few medicinal remedies with which we are accustomed to meet the same symptoms under other circumstances.

The great number of deaths arising from fatty heart, heart paralysis, arteriosclerosis, and dropsy are not ordinarily to be regarded as unavoidable consequences of disease, but for the most part are the result of conditions which the patient has brought upon himself and which he can avert by the use of sure means and methods, even in the advanced stages, if he has the will power to do so. In this regard he is the master of his own health.

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